

# Pseudoepitheliomatous Hyperplasia After Excision of a Pleomorphic Adenoma from the Hard Palate: Case Report

## Sert Damaktan Pleomorfik Adenom Eksizyonunun Ardından Psödoepitelyomatöz Hiperplazi

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**ABSTRACT** Pseudoepitheliomatous hyperplasia is a reactive epithelial proliferation of mucosal and cutaneous epithelium. The differential diagnosis of pseudoepitheliomatous hyperplasia from squamous cell carcinoma may be difficult. Pseudoepitheliomatous hyperplasia is a benign lesion, which may be treated with conservative local excision, while squamous cell carcinoma is a malignant tumor, which requires aggressive surgery. Therefore, the differential diagnosis is essential in order to avoid radical surgery. Immunohistochemical stains may be useful as a diagnostic adjunct in cases where it is difficult to distinguish a benign process from a malignant one. This case report presents a 75-year old patient with pseudoepitheliomatous hyperplasia at the excision area of a pleomorphic adenoma in the hard palate and relevant diagnostic challenges.

**Key Words:** Palate, hard; adenoma, pleomorphic; squamous cell carcinoma

**ÖZET** Psödoepitelyomatöz hiperplazi, mukozal ve kutanöz yüzey epitelinin reaktif epitelyal çoğalmasdır. Psödoepitelyomatöz hiperplazinin skuamöz hücreli karsinomdan ayırıcı tanısı zor olabilir. Psödoepitelyomatöz hiperplazi benign bir lezyondur ve tedavisi konservatiftir; skuamöz hücreli karsinom ise malign bir tümördür ve tedavisi genellikle agresif cerrahi gerektirir. Bu nedenle radikal tedaviden kaçınmak için ayırıcı tanı çok önemlidir. Benign oluşumun malignden ayrılmasının zor olduğu durumlarda immünohistokimyasal boyalar, tanıda yardımcı olabilir. Bu olgu sunumunda, 75 yaşındaki hastada, sert damaktaki pleomorfik adenomun eksizyon alanında psödoepitelyomatöz hiperplazi ve onun tanısal zorlukları sunulmuştur.

**Anahtar Kelimeler:** Sert damak; adenom, pleomorfik; skuamöz hücreli karsinom

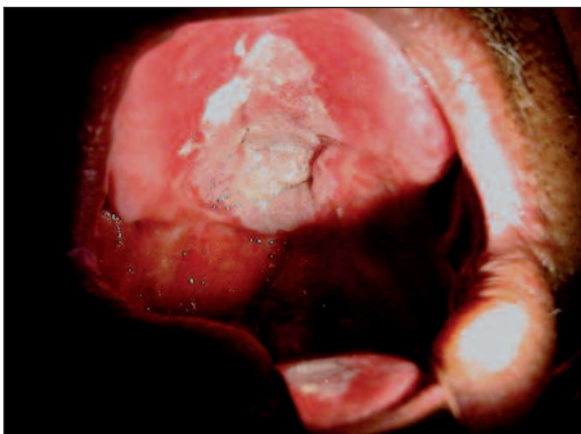
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**P**seudoepitheliomatous hyperplasia (PEH) or pseudocarcinomatous hyperplasia is characterized with a downward proliferation of the epidermis into the dermis or the mucous epithelium and the subepithelial connective tissue.<sup>1-4</sup> PEH resembles squamous cell carcinoma (SCC) both clinically and histologically and may be misinterpreted as SCC.<sup>1,2,5</sup>

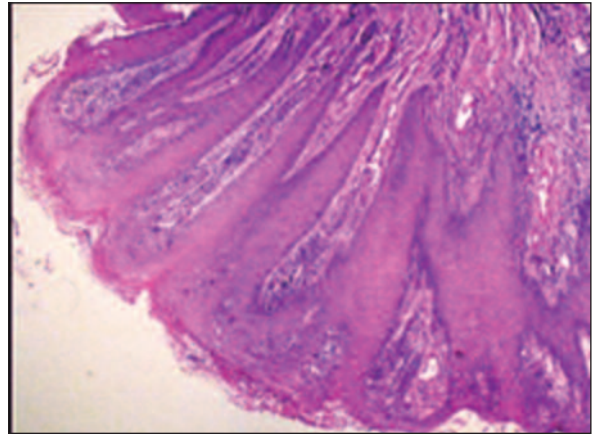
PEH is a benign lesion and its treatment is usually conservative, while SCC is a malignant tumor, which usually requires aggressive surgery. Therefore, the differential diagnosis is essential in order to avoid unnecessary and radical therapy. Herein, we described a case of PEH with fungal infection after excision of a pleomorphic adenoma of the hard palate.

## CASE REPORT

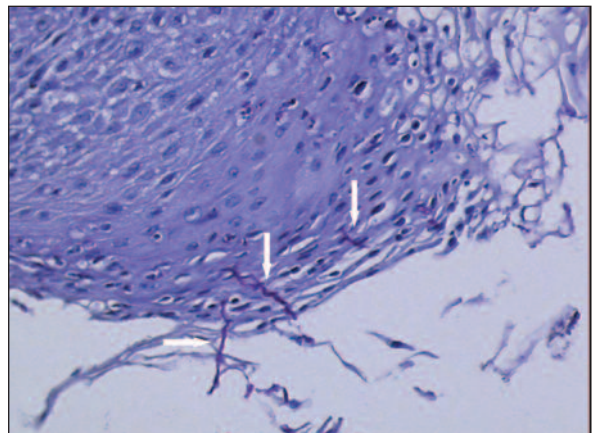
A 75-year-old male patient presented to our clinic with a progressive and painless mucosal lesion on the hard palate that had initially appeared 3 weeks ago. The patient had undergone surgery nine months ago at the same anatomical area for a pleomorphic adenoma that had been excised with clear margins. He had no history of a systemic disease other than hypertension. No history of cigarette smoking or alcohol use was present. Intraoral examination showed an irregularly circumscribed ulceration at the previous excision area on the hard palate. The margins were slightly elevated and the surface was marked with grayish debris (Figure 1). At first sight, the lesion looked like primary squamous cell carcinoma or a carcinomatous transformation of the previously treated pleomorphic adenoma. Therefore, a punch biopsy was performed under local anesthesia. Microscopic examination of the specimen revealed active chronic inflammation and granulation tissue areas. Downward proliferation of the epithelium was also noted (Figure 2). Furthermore, numerous fungal hyphae were detected on the surface of the epithelium (Figure 3). The histopathologic diagnosis was PEH with fungal infection. The patient was treated with antifungal (Nystatinsuspension) medication. The patient was free of the disease 4 weeks after medical therapy. There was no recurrence during the 12-months follow-up period.



**FIGURE 1:** Macroscopic appearance of the active chronic inflammation and infection caused by fungus on the palatal mucosa after excision. (See for colored form <http://tipbilimleri.turkiyeklinikleri.com/>)



**FIGURE 2:** Polypoid architecture of the lesion. Pseudoepitheliomatous hyperplasia and active chronic inflammation are noted (HE, x25). (See for colored form <http://tipbilimleri.turkiyeklinikleri.com/>)



**FIGURE 3:** Fungal hyphae (arrows) are visible on the surface of the epithelium (Periodic acid-Schiff X200). (See for colored form <http://tipbilimleri.turkiyeklinikleri.com/>)

## DISCUSSION

Pseudoepitheliomatous hyperplasia is a reactive epithelial proliferation of mucosal and cutaneous surface epithelium.<sup>2</sup> While typically observed in wound healing reactions, especially in re-excision specimens, this phenomenon may be diagnosed in a wide variety of clinical conditions, including inflammatory and degenerative diseases, and infectious processes especially caused by fungal agents.<sup>3,6</sup> Although the majority of the cases develop on the skin, PEH has also been reported in various locations of the oral cavity, including the gingiva, tongue, and palate with intramucosal nevi, spitz nevi, and melanoma.<sup>2,3</sup> In addition, PEH may arise

on the mucosal surfaces including the hard palate after resection for pleomorphic adenoma, and this rare entity may mimic carcinoma, which was our first clinical diagnosis at first sight.

Although PEH is a well-known phenomenon, its pathogenesis is poorly understood.

That is a question why a non-neoplastic epithelium strays from its borders and resembles carcinomatous tissue by presenting invasive patterns. In cases of pseudoepitheliomatous change, it is suggested that the orderly relation between the epithelial and fibroblastic activities is altered and wild proliferation of the epithelial elements and chronic granulomatous mesoderm growth occur simultaneously.<sup>7</sup> Prolonging the inflammation phase of the healing process, infection is assumed to be the major cause of PEH. Inflammatory cytokines (particularly cytokines 1, 10 and 14) may also play a role in the development of PEH.<sup>8</sup>

Histological examination of PEH typically reveals pronounced epidermal hyperplasia with irregular jagged epidermal downgrowth into the underlying dermis or the mucous epithelium and the subepithelial connective tissue.<sup>2,3,5</sup> Deeper in the dermis or submucosa, a dense inflammatory infiltrate of neutrophils and histiocytes is noted. The most significant diagnostic features of PEH are the absence of nuclear atypia, abnormal mitoses, or individual dyskeratotic keratinocytes. Conversely, the presence of nuclear pleomorphism, atypia and mitotic activity appear in squamous cell carcinoma (SCC).<sup>2,5,9</sup> Special stains for infectious agents and microbiological studies may be helpful to reveal co-existing infectious organisms.

In the presented case, active-chronic inflammation and granulation tissue, downward proliferation of the epithelium, fungal hyphae on the surface of the epithelium were noted (Figure 2, 3).

Due to both clinical and histological similar appearance to SCC, PEH may be misdiagnosed as SCC.<sup>1,2,5</sup> Especially if the biopsy is taken superficially and the tissue sample is not adequate, exclusion of carcinoma can be very difficult. Recognition of the underlying lesion, preferential proliferation of adnexial epithelial cells, confinement of the proliferation of the papillary dermis, slight cytological atypia with absence of large nucleoli, few or absent mitotic figures, little or no single cell necrosis, and little tendency to horn pearl formations have been described as criteria for differentiating pseudoepitheliomatous hyperplasia from invasive SCC.<sup>10</sup> However, Wolber et al. reported that the only feature present in SCC, but absent in pseudoepitheliomatous hyperplasia, was severe epithelial cell atypia and claimed that the majority of these criteria were not reliable.<sup>11</sup> Besides, p53 and matrix metalloproteinase 1 staining was significantly increased, while E-cadherin staining was decreased in SCC compared to PEH.<sup>5</sup> Therefore, immunohistochemical stains may be useful as a diagnostic adjunct in cases where it is difficult to distinguish a benign process from a malignant one.

## CONCLUSION

Being a benign entity, which is typically induced by prolonged infection and treated medically, PEH should be considered in the differential diagnosis of SCC, that requires aggressive treatment modalities. Collaboration between the clinician and pathologist is crucial to avoid unenviable consequences.

## REFERENCES

1. Suzuki T, Kumamoto H, Nagasaka H, Kawamura H, Ooya K. Intramucosal naevus with pseudoepitheliomatous hyperplasia in the gingiva: a case report. *Int J Oral Maxillofac Surg* 2002;31(3):330-3.
2. Meleti M, Mooi WJ, van der Waal I. Oral malignant melanoma associated with pseudoepitheliomatous hyperplasia. Report of a case. *J Cutan Pathol* 2006;33(4):331-3.
3. Takeda Y, Sasou S, Obata K. Pleomorphic adenoma of the minor salivary gland with pseudoepitheliomatous hyperplasia of the overlying oral mucosa: report of two cases. *Pathol Int* 1998;48(5):389-95.
4. Goel R, Wallace ML. Pseudoepitheliomatous hyperplasia secondary to cutaneous aspergillus. *Am J Dermatopathol* 2001;23(3):224-6.
5. Zarovnya E, Black C. Distinguishing pseudoepitheliomatous hyperplasia from squamous cell carcinoma in mucosal biopsy specimens from the head and neck. *Arch Pathol Lab Med* 2005;129(8):1032-6.
6. Kheir SM, Flint A, Moss JA. Primary aspergillosis of the larynx simulating carcinoma. *Hum Pathol* 1983;14(2):184-6.

7. Ju DM. Pseudoepitheliomatous hyperplasia of the skin. *Dermatol Int* 1967;6(2):82-92.
8. Kaminagakura E, Bonan PR, Lopes MA, Almeida OP, Scully C. Cytokeratin expression in pseudoepitheliomatous hyperplasia of oral paracoccidioidomycosis. *Med Mycol* 2006;44(5):399-404.
9. Hanly AJ, Jorda M, Elgart GW. Cutaneous malignant melanoma associated with extensive pseudoepitheliomatous hyperplasia. Report of a case and discussion of the origin of pseudoepitheliomatous hyperplasia. *J Cutan Pathol* 2000;27(3):153-6.
10. Grunwald MH, Lee JY, Ackerman AB. Pseudocarcinomatous hyperplasia. *Am J Dermatopathol* 1988;10(2):95-103.
11. Wolber RA, Talerman A, Wilkinson EJ, Clement PB. Vulvar granular cell tumors with pseudocarcinomatous hyperplasia: a comparative analysis with well-differentiated squamous carcinoma. *Int J Gynecol Pathol* 1991;10(1):59-66.