

侵犯上唇的壞死性涎腺化生：披著狼皮的羊

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Necrotizing Sialometaplasia Affecting the Upper Lip: A Sheep in Wolf's Clothing

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Necrotizing sialometaplasia (NS) is a self-limited inflammatory disease mainly involving minor salivary glands. The clinical and histological resemblance to malignancy, such as squamous cell carcinoma and mucoepidermoid carcinoma, makes this entity important. Lips are rarely involved. A 39-year-old man presented with a deep-seated nodule with central ulceration of the upper lip for a three-month duration. The tumor was biopsied followed by excision after an initial report of low-grade mucoepidermoid carcinoma. Histology of the tumor revealed necrosis of salivary glands, squamous metaplasia of salivary ducts and acini with bland appearance of the squamous cells which showed occasional nuclear atypia. The preservation of an overall lobular morphology was found, a hallmark feature of NS allowing its differentiation from malignancy pathologically. The etiology of NS is widely accepted as infarction of the glands resulting from ischemia. NS generally heals spontaneously without treatment in six to ten weeks. The NS in the present case is unusual in that it affected the lip; it thus presents as a great diagnostic challenge to both dermatologists and pathologists. An awareness of NS is important so that over-diagnosis and over-treatment of the condition as malignancy can be avoided. (Dermatol Sinica 22 : 88-92, 2004)

Key words: Necrotizing sialometaplasia, Mucocutaneous carcinoma, Squamous cell carcinoma, Squamous metaplasia

壞死性涎腺化生是一種具有自限性的發炎疾病，主要侵犯小唾腺。本疾病的重要性，在於臨床及病理表現都與惡性腫瘤相似，尤其是鱗狀細胞癌和黏液表皮樣癌。通常很少侵犯唇部。一個39歲的男病人，在上唇深處有一顆持續三個月的結節，後來其表面的中央產生潰瘍。切片檢查其初步報告為低惡性度之黏液表皮樣癌，之後即切除整個病灶。病理特徵為：唾腺壞死、唾腺管與腺泡的鱗狀化生、其鱗狀細胞外觀平淡無奇，但偶可見異常細胞核。而

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維持整個唾腺的小葉型架構，是壞死性涎腺化生在病理上能與惡性腫瘤區別的主要特徵。其最廣為接受的病因是腺體的梗塞形成，導因於缺血的變化。即使不治療，也通常在六至十週內自然痊癒。壞死性涎腺化生發生於唇部並不常見；對於皮膚科及病理科醫師都是診斷上的一大挑戰。注意是否有壞死性涎腺化生是很重要的，如此才可以避免誤認為惡性腫瘤的過度診斷及過度治療。(中華皮誌22：88-92, 2004)

INTRODUCTION

Necrotizing sialometaplasia (NS) is a self-limited, inflammatory disorder with clinical and histological features that greatly simulate malignancy.¹ NS mainly involves the minor salivary glands. But cases of NS involving the lips are extremely rare.² Recognition of such uncommon location is important so that unnecessary surgery can be avoided. In this report, we describe a case of NS involving the upper lip and review the English literature.

CASE REPORT

A 39-year-old Taiwanese man was admitted for a three-month history of a painless and slow-growing nodule on the upper lip, on which a painful necrotic ulcer had developed one week prior to admission (Fig. 1). The patient, an outdoor worker, had smoked approximately one pack of cigarettes daily for twenty years. Past medical history, and review of system were unremarkable. There was no history of chronic



Fig. 1
A necrotic ulceration presents over the preexisting nodule on the vermilion border of the left side of upper lip.

alcohol consumption. He denied recent trauma, radiation or surgery in the oral sites. A provisional clinical diagnosis of lip carcinoma was made. An incisional biopsy with elliptic shape (1.0 cm x 0.5 cm x 0.3 cm) was performed. The initial pathological examination suggested a low-grade mucoepidermoid carcinoma because of a few tumor nests combined both well-differentiated squamoid and mucoid cells in the dermis. As a result, conservative excision was performed after biopsy.

The surgical specimen was reviewed again

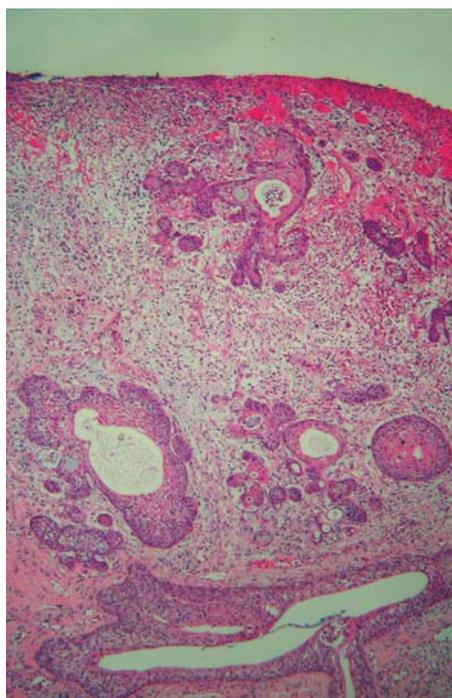


Fig. 2
The surface epithelium is ulcerated. Lobular distribution of the metaplastic squamous nests retaining ductal lumina is seen in the dermis. Diffuse inflammatory infiltrate is noted.

after excision. Histopathological examination showed an ulcerated surface. In the underlying dermis, there was some irregular proliferation of squamous nests and focal necrosis of minor salivary gland lobules and ducts. There were both an acute and chronic inflammatory infiltration and granulation tissue surrounding the lesion.(Fig. 2) Some of the squamous nests retained the residual ductal lumina or mucoid glandular cells. These changes were interpreted as squamous metaplastic change in the ducts and acini of minor salivary glands. A few squamous nests coexisted with the normal-appearing salivary acini.(Fig. 3) It was evident that squamous metaplasia of the minor salivary glands was a reactive process. At higher magnification, some foci of reactive nuclear atypia were found within the bland-looking metaplastic squamous nests.(Fig. 4) However, the hallmark of pathologic diagnosis was the preservation of the overall lobular architecture of the involved minor salivary glands.(Fig. 2) Based on clinical appearance and characteristic histopathological features, the diagnosis was revised to NS on review. No new lesion had been found during the follow-up period of three months.

DISCUSSION

NS is a reactive process involving salivary glands that is easily confused with malignancy. It was first reported as a distinct entity by

Abrams *et al.* in 1973.³ In their report, NS only involved minor salivary glands. Subsequently, NS has been described in other parts of the oral cavity, in major salivary glands, and in the upper respiratory tract.⁴ Undoubtedly, before the recognition of NS, many patients received unnecessarily mutilating surgery because of its resemblance to malignancy, particularly squamous cell carcinoma and mucoepidermoid carcinoma. NS is definitely a sheep in wolf's clothing, as Robert *et al.* commented in 1986.⁵

NS is an uncommon disease with an estimated prevalence of 0.03% of all lesions in the oral cavity submitted to pathologic examination.⁶ The majority of cases of NS involved the intraoral minor salivary glands, primarily those of the hard palate (77%).⁴ Lips are rare location affected by NS. In review of English literature, only 12 cases of NS of the lips have been reported.^{2, 4, 7-9} The average age at diagnosis was 45.9 years. Males outnumbered females by a ratio of 1.9:1.⁴

Clinically, NS most frequently presented as a deep-seated ulcer, with or without a preceding swelling or nodule. A nonulcerated swelling or nodule accounts for only one third of all cases.¹ Painful lesions are twice as common as asymptomatic ones.⁴ Paresthesia or anesthesia may also be noted and contribute to the confusion of NS with a malignant neoplasm.¹⁰ The useful clinical clues to the benign nature of NS are

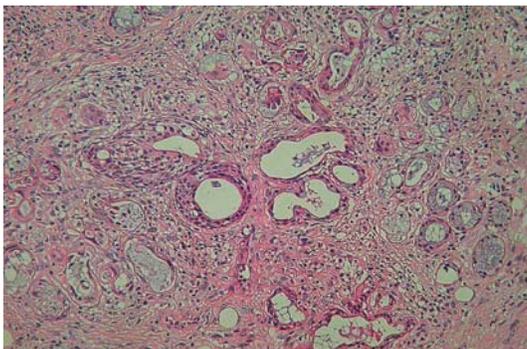


Fig. 3
Deep-seated squamous metaplasia and residual ductal lumina are adjacent to the necrotic but relatively normal-appearing acini.

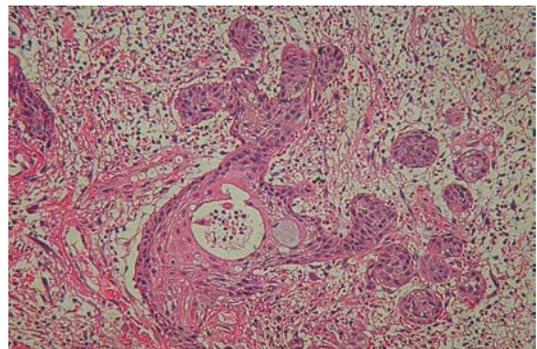


Fig. 4
A deeper lobule shows extensive squamous metaplasia and benign nuclear morphology. Some foci of reactive nuclear atypia are present.

rapid presentation of the lesion and evidence of healing after only a brief period of observation (one to two weeks).⁵

Histological features show coagulative necrosis of salivary gland lobules and squamous metaplasia within adjacent viable lobules. Abrams *et al.* proposed helpful criteria for differentiating NS from malignant lesions.³ They are: (1) lobular infarction or necrosis; (2) bland-appearing nuclear morphology of the squamous cells; (3) simultaneous metaplasia of ducts and mucous acini; (4) prominent granulation tissue and inflammatory component, and (5) maintenance of general lobular morphology in spite of fairly extensive inflammatory and metaplastic changes often involving more than one lobule. Faintly basophilic sialomucin may be seen within the necrotic glands. It is both PAS-positive and alcian-blue-positive. Normal-appearing salivary acini may coexist with the necrotic glands.¹¹ It represents an important evidence of a reactive process, not a neoplasm.

NS should be differentiated from mucoepidermoid or squamous cell carcinoma. Its deep-seated location and infiltrating border of squamous nests resemble the tumor islands of squamous cell carcinoma.¹¹ The coexistence of squamoid and mucoid cells in the tumor-like nests may lead to misdiagnosis as mucoepidermoid carcinoma. The squamous metaplasia of ducts and acini can be associated with prominent nuclei and frequent mitotic figures.¹ In these situations, the preservation of lobular appearance and the presence of intraepithelial inflammation in the squamous nests are the most important criteria in establishing the correct diagnosis.⁴

Robert *et al.* pointed out that 11.4% of patients with NS received unnecessary therapy as a result of incorrect microscopic interpretation.⁴ The majority of misdiagnosis was the malignant tumors. There is no any immunohistochemistry technique to date is announced to be beneficial in the diagnosis of NS. Thus a sufficiently deep incisional biopsy is of paramount importance.⁸ An adequate biopsy, large enough to show the general lobular morphology, cou-

pled with careful histologic analysis can exclude malignancy.^{8, 12} If the surgical specimen is too small and clinically spontaneous resolution is apparent, repeat biopsy is a wise choice.

Ischemia of the blood supply in the salivary glands is the most widely accepted pathophysiologic theory.¹² This theory is supported by animal experiment. NS can be produced in rats by ligating the vasculature supplying the submandibular and sublingual salivary glands. The possible predisposing factors resulting in ischemia are traumatic injury, dental injection, ill-fitting dentures, smoking, alcohol consumption, radiation, upper respiratory infection, allergy, or recent surgery in the oral sites.^{4, 12}

NS is a self-limited disease. It generally resolves spontaneously without treatment within 6 to 10 weeks.^{4, 13} Appropriate management consists of adequate incisional biopsy, observation and reassurance, and symptomatic treatment. Repeat biopsy is indicated when no evidence of resolution is noted at two weeks of follow-up.^{5, 14} In summary, we described a case of NS occurring in the upper lip. Lips are unusual location for NS; such cases present a diagnostic challenge to both clinicians and pathologists. An awareness of NS is critical to prevent over-diagnosis and over-treatment as squamous cell carcinoma or mucoepidermoid carcinoma.

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