

# A Verruciform Xanthoma of the Lower Lip and Review of the Differential Diagnosis

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## Abstract

A careful examination of lips is often neglected by the members of the medical and dental professions; yet the lips reveal a heterogeneous group of lesions ranging from congenital abnormalities to benign and malignant neoplasms. Verruciform Xanthoma (VX) is an uncommon benign inflammatory mucocutaneous condition that occurs in the oral cavity which was first described by Shafer in 1971. It is often associated with pre-existing epithelial and/or inflammatory disorder and is characterized histopathologically by papillary epithelial hyperplasia and the presence of foamy macrophages in connective tissue papillae. We report a case with VX which presented as a well-defined, soft, painless swelling on the lower lip having different clinical features.

**Key Words:** *Verruciform, Xanthoma, Foam cells, Oral mucosa*

## Clinical Presentation

A 35 year old male patient reported to the department of oral medicine with a swelling on the right half of the lower lip noticed since 1.5 years. The swelling was gradual in onset, slowly progressing in size with no pain, altered sensation and did not interfere with function. The patient's medical history revealed blurred vision noticed since childhood and surgery of the right eye for cataract 10 years ago. Examination of the lesion revealed well defined roughly oval swelling approximately 1x1 cm in size covered by mucosa that was normal in texture and colour (*Figure 1*). On palpation freely moveable mass was noted which was soft fluctuant and non-tender with no signs of paresthesia or hypesthesia.

No similar lesions were noticed elsewhere on the body. On examination of dentition full complement of erupted permanent teeth were noted with root stump in relation to 41, microdontia in relation to 31, Deep dental caries in relation to 37 and initial dental caries with 16, 36, 47. Patient did not give any history of trauma to the lower lip due to root fragment, Routine blood investigations like complete haemogram, Erythrocyte Sedimentation Rate (ESR) and blood glucose levels were within normal limits.



*Figure 1.* A well-defined swelling on the lower lip.

## Differential Diagnosis

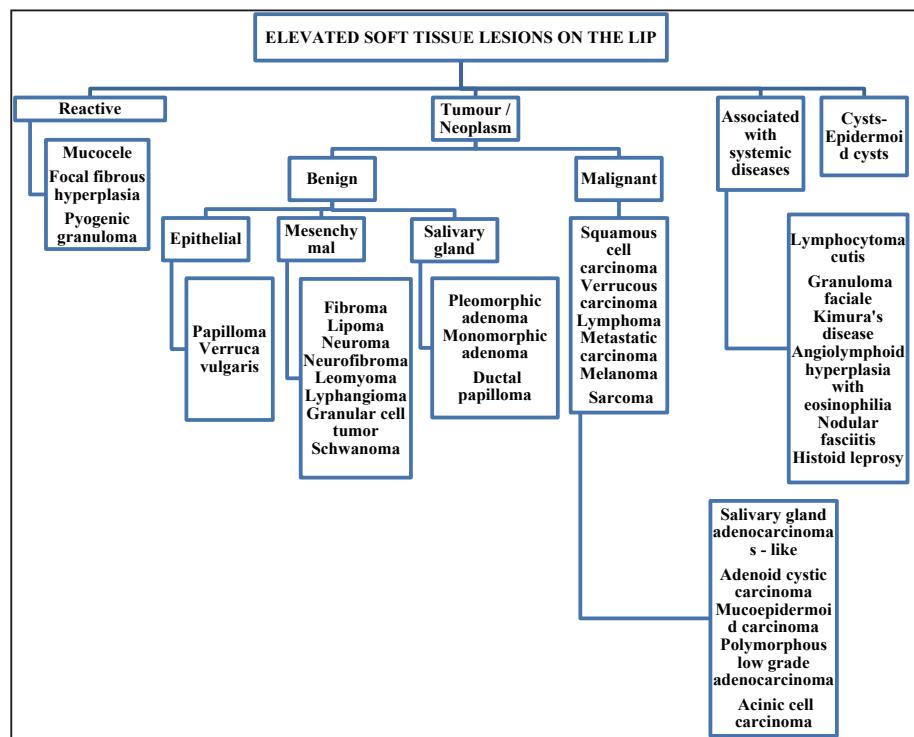
Elevated soft tissue lesions of the lip can occur in various pathologic conditions and may be present for a prolonged period of time before the patient seeks medical advice, usually when the lesion interferes with functions of lip or esthetics. A broad classification of these elevated lesions of the lip is illustrated in *Figure 2*. Based on the clinical appearance, origin of these pathologies may be determined. Lesions of epithelial origin typically present as exuberant tissue proliferation producing papillary or verruciform configuration. Lesions of mesenchymal origin arise below the epithelium and appear as dome-shaped swellings. The overlying epithelium is often intact, but its coloration reflects the contents of the lesion: red-purple if vascular, blue if mucinous or yellow if adipose, lymphoid or neural. Reactive lesions and soft tissue cysts also present as dome shaped swellings. Malignant lesions present as rapidly growing irregular mass which may be indurated involving deeper tissues.

Based on the dome shaped appearance of presented case, our differential diagnosis included reactive lesions like focal fibrous hyperplasia, mucocele, matured pyogenic granuloma, benign mesenchymal lesions, minor salivary gland tumors and soft tissue cyst like epidermoid cyst.

Focal fibrous hyperplasia (also known as Nodular hyperplasia, Traumatic fibroma or irritational fibroma) is the most common soft tissue lesion of normal colour encountered in the oral cavity and can occur frequently on the lips. It is usually initiated by trauma such as lip biting. It is not a true neoplasm and has limited growth potential, rarely exceeding 1-2 cm in diameter. It grows slowly, varies in consistency from soft to firm and regresses or disappears when the offending irritant is eliminated [1]. The present case was considered most likely the representation of nodular hyperplasia because of site involved and clinical appearance.

Mucocele was considered next in the differential diagnosis as it is a common lesion of the lower lip that appears dome shaped and varies from 1 – 2 mm to several centimeters. The typical lesion appears as an elevated vesicular or bullous lesion with slightly bluish or translucent appearance due to vascular

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**Figure 2.** Classification of elevated soft tissue lesions of the lip.

congestion, tissue cyanosis above and fluid accumulation below. The thin overlying mucosa permits the pool of mucous fluid to absorb most of the visible wavelengths of light except the blue, which is reflected. But it may show normal mucosal pink colour when it is situated deeper in the tissues because of the thickness of covering mucosa. These are characteristically fluctuant but some are firm on palpation and frequently resolves spontaneously [1-7]. The clinical appearance of our case was compatible with a deeply situated mucocele but it has not resolved spontaneously.

Pyogenic granuloma is an inflammatory fibrous hyperplastic lesion, is clinically asymptomatic reddish papule nodule or polyp which usually shows at least part of its surface to be rough and ulcerated. The most common location is gingiva particularly in the anterior region. Other locations are lips, tongue, buccal mucosa, palate, vestibule and alveolar mucosa in edentulous regions [1]. Possibility of pyogenic granuloma in the present case was less likely due to absence of reddish ulcerated surface. However, matured pyogenic granulomas may present as, non-ulcerated elevated lesion covered by normal appearing mucosa and hence was considered among differential diagnosis.

Intra oral lipomas generally are slow-growing, well-circumscribed, painless soft tissue tumors occasionally occurs on mucosal surface of the lip that may be superficially or more deeply located. It may occur as sessile or pedunculated mass covered by atrophic epithelium with the underlying adipose tissue often giving the lesion a classic yellowish appearance. Lipomas are most commonly soft and sometimes almost fluctuant to palpation. The present case demonstrates similar clinical presentation of lipoma but it did not show yellowish clinical appearance [1,8-10].

Hemangiomas may also present as elevated lesions on the lip. These are benign vascular alterations characterized by proliferation of blood vessels, commonly occurring in

subcutaneous and submucous tissue, typically exhibit purplish color and may reduce in size due to emptying of its blood vessels [11-16]. However, deeply situated Intramuscular hemangioma does not exhibit the classic color change and hence can be difficult to diagnose. Imaging modalities like ultrasonography and Magnetic resonance imaging are required for the confirmation of these lesions. .

Oral Focal Mucinosis (OFM) is an uncommon clinicopathologic condition that is considered to be the oral counterpart of cutaneous focal mucinosis. It is a disease of unknown etiology possibly resulting from overproduction of hyaluronic acid. Clinically these lesions present as sessile or pedunculated painless nodular mass that are same colour as surrounding normal mucosa. Surface is typically smooth non ulcerated, although occasional cases exhibit lobulated appearance. Size varies from few millimeters to 2 cm. The patient may be aware of mass for many months to years before the diagnosis is made [17].

Neurofibroma is a benign tumor of neural tissue. It frequently involves skin and rarely oral mucosa. Neurofibromas of the lip are discrete, non-ulcerated nodules, which tend to be of same color of normal mucosa. Usually occurs on buccal mucosa, palate, alveolar ridge, vestibule and tongue; also reported in lips and gingiva [18,19].

Adenomatoid Hyperplasia (AH) is a non-neoplastic enlargement of minor salivary glands. Clinically, the lesion presents as an asymptomatic, firm, sessile and non-tender, nodular mass that is not ulcerated. It is most commonly seen on the palate, but other sites like buccal mucosa, upper lip, retromolar region and lower lip were also found to be affected. The condition has been regarded as idiopathic, but the role of chronic trauma has been suggested [20].

Epidermoid cysts can be classified as either congenital or acquired. Congenital types are thought to develop from congenital inclusions of ectodermal tissue during

embryologic development, whereas acquired variants are believed to originate through implantation of epithelium, by either surgical or accidental trauma into deeper mesenchymal tissues. Some (25%) of these head and neck cysts develop in the floor of the mouth, with the remainder generally found in the tongue, lips, palate and jaws. Epidermoid cysts on the lip were reported as soft, non-tender, fluctuant roughly round and well circumscribed lesions which are compatible findings seen in present case [21].

Cystecercosis is a parasitic infestation by the larval stage of the pork tapeworm *Tenia solium*. Infection with cystecercosis may involve many parts of the body including the subcutaneous tissues, eyes, heart, liver, lungs and peritoneum. However, the most commonly affected site is skeletal muscle. The most frequently involved oral locations are the tongue, labial or buccal mucosa and floor of the mouth. Oral presentations are in the form of painless, well circumscribed, soft swelling that may mimic fluctuant lesions like mucocele [22].

Early benign and malignant minor salivary gland are usually nodular or dome-shaped elevations with smooth contours and the overlying mucosa is normal or appears smoother and glossier because of the tension created by underlying expanding tumor. Minor salivary gland tumors are often fully movable, spherical or ovoid masses when they are located on the lining mucosa. The posterior palate is most common site of their occurrence but can also occur on other areas like buccal mucosa, retromolar region and upper lip. Few cases were located on the tongue, gingivae, bone, lower lip and floor of the mouth [1].

Well differentiated mucoepidermoid carcinoma, mucous producing adenocarcinoma and papillary cystadenoma lymphomatous (Warthin's tumor) are the minor salivary gland tumors which exhibit moderately soft consistency and are frequently fluctuating to palpation. The softness of these tumors results from the lack of dense cell aggregates, the fluid produced and the consequent retention phenomenon [1].

Other than these there are certain painless, well circumscribed, elevated, soft lesions on the lip that occur rarely on the lower lip which are reported in the literature like pleomorphic adenoma, solitary fibrous tumor, schwannomas, minor salivary gland calculi, varix and Verruciform Xanthoma.

Pleomorphic adenoma is the most common neoplasm of the minor salivary glands which are uncommon among the entire salivary gland tumors. The lower lip is a very rare site of occurrence for pleomorphic adenoma [23].

Solitary Fibrous Tumor (SFT) is a rare mesenchymal neoplasm, previously nomenclatured as localized benign mesothelioma, submesothelioma, or localized fibrous tumor of the pleura [24]. It is an extremely rare lesion, which may account for about 3% of the SFT cases in the whole body. SFT involvements of the salivary gland have been reported to be even rarer [25].

Schwannomas occurring intra-orally (about 1%) constitute 45.2 to 52% on tongue, 13.3% on cheek, 19.86% on buccal/vestibular mucosa and 19.24% on lip and gingiva, hence occurrence of schwannoma on lower lip is rare [26,27].

Minor salivary gland calculi occur primarily in the upper lip of patients in fifth and seventh decades. Most appear as

firm to hard, movable submucosal nodules. Lesions vary from 3-15 mm in diameter; majorities are less than 5 mm. Etiologic factors include unusual morphologic features of the involved duct and local trauma [28].

Varix (VAR) is an acquired benign vascular lesion, generally asymptomatic, and does not require treatment. Age is a predisposing factor, as well as tissue loosening and increased venous pressure. Oral VAR is very common in old adults. Oral VAR is characterized as a red to purple papule or nodule, commonly found on the tongue, lip or cheek, mainly in the seventh decade of life. Also, there are few studies on epidemiological data on oral VAR [29].

Verruciform Xanthoma (VX) is a relatively rare benign lesion and occurs in the oral cavity predominantly, which occasionally affects skin and genital mucosa. It appears as a papule or single plaque showing a verrucous or papillomatous aspect, with variable color from reddish pink to gray. In majority of oral cases, it affects gingiva and alveolar mucosa such a solitary lesion [30].

Malignant soft tissue tumors were considered to be a remote possibility for the present case. Rapid growth, lack of circumscription, fixation to adjacent structures, and ulceration of the overlying mucosa are common features of malignancy that were not noted in the present patient.

## Diagnosis and Management

Patient underwent excision of the lesion under local anesthesia and aseptic precautions. Curvilinear incision at the posterior border of lesion was given to expose the lesion, lesion was separated with help of blunt dissection followed by complete excision of lesion and primary closure was carried out. Intra operatively the mass appeared well encapsulated and was easily separable from the surrounding tissues. It was totally excised and the surgical specimen was roughly round soft tissue mass with a thick capsule. The patient had an uneventful postoperative recovery.

The lesion was totally excised and submitted for histopathologic examination. The clinical diagnosis was given as focal fibrous hyperplasia. The specimen was processed for routine hematoxylin and eosin staining.

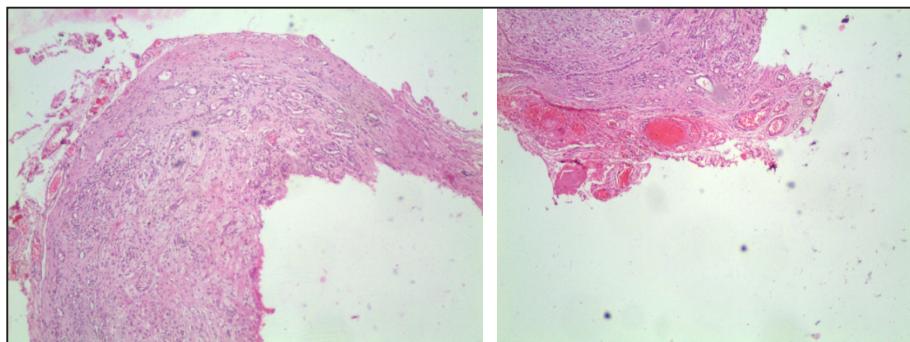
Microscopic examination revealed parakeratinized epithelium with papillary projections and underlying connective tissue stroma contained nests of large cells having clear cytoplasm and round nuclei, some with prominent nucleoli called foam cells or xanthoma cells and showed mild to moderate inflammatory cell infiltration predominantly lymphocytes. There was no evidence of dysplasia or malignancy (*Figures 3 and 4*).

Based on these histopathological findings, final diagnosis of verruciform xanthoma was made.

The patient had been under regular follow-up for 2 years and remained free of recurrence or presence of new lesion.

## Discussion

Verruciform Xanthoma (VX) is an uncommon, benign, and usually solitary papillary lesion with a predilection for oral mucosa [31]. It was first reported in 1971 by Shafer who described 15 cases occurring in the oral mucosa [32]. The frequency of occurrence is from 0.025 to 0.094% and may



**Figures 3 and 4.** Photomicrographs.

also affect the skin especially of the genital area [33,34]. VX affects mostly adults in the 4<sup>th</sup> and 5<sup>th</sup> decades without sex predilection [31,35,36].

VX occurs mainly in the oral cavity, although it may arise from any surface or lining epithelium such as vulva, scrotum, and skin. VX manifests as an asymptomatic solitary, slow-growing plaque or nodule with a papillary, granular or verrucous surface and sharply delineated margins that may appear pink, red, yellow, or white in color [31]. The occurrence of multiple or disseminated VX is extremely rare [37-39]. Approximately 75% of all oral VX lesions occur on the masticatory mucosa of the palate, gingiva or the alveolar ridge [31].

The etiopathogenesis of VX is unclear but appears to be associated with localized inflammation [40]. Immunologic factors and viral etiologies have been also suggested [35,40]. The prevailing theory is that epithelial tissue damage results in the breakdown of the phospholipid-rich cell membranes releasing lipids that are then taken up by macrophages in the connective tissue that become lipid-laden or foamy in appearance [41-43]. An immunologic pathogenesis has been suggested because of the predominant T cells infiltrate, and decreased number of Langerhans cells in oral VX compared to normal tissue [44,45].

Xanthomas represent the accumulation of lipid-rich histiocytes (macrophages) known as foam cells. The lipids in xanthomas are primarily free and esterified cholesterol, but occasionally other sterols and even triglycerides accumulate. Due to high plasma concentration, there is subsequent permeation of lipoproteins through the walls of capillaries. The lipid is taken up by macrophages, which evolve into

foam cells. Xanthomas are usually associated with disorders of lipoprotein metabolism [46]. It has also been suggested that degenerative changes in the epithelium lead to the presence of foam cells.

Investigations about matrix metalloproteinase (MMP-2 and -9) and the accumulation of foam cells in VX lesions revealed that the latter is mediated partly by an immune mechanism associated with MMPs, which degrade basal membrane of the epithelium and promote a reciprocal induction between the mesenchymal and epithelial cells. Ide et al. have suggested that under synergistic regulation of T cells, macrophage recruitment in the sub-basal mesenchyme and the lysosomal engulfment of epithelial lipids by macrophages are essential in the formation of the VX lesion [47,48].

Three histological subtypes (types A, B, and C) have been described based on the texture of the surface epithelium. Lesions of the verrucous type (A) have hyperparakeratosis, verrucous type acanthosis, and elongation of the rete ridges. The papillary form (B) has many finger-like projections composed of stratified squamous epithelium containing connective tissue cores. In the flat type (C), mild acanthosis and subtle thin parakeratosis with variable elongation of rete ridges are commonly observed [31,48].

This case report illustrates the rare site of presentation of Xanthoma occurring on lower labial mucosa which was diagnosed and managed efficiently at initial stage in our institution. We conclude that well defined, soft, painless swellings present on lower lip are not always commonly occurring entities and need more attention for diagnosis and management.

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