

cytoplasm, with large, spherical, vesicular nuclei. The cells were arranged in large or small solid alveoli, trabecular, or sheets that were associated to thin-walled blood vessels often lined by tumor cells. The tumor, when immersed in dichromate solution, took on a characteristic dark brown appearance due to the base of the chromaffin reaction of the tumor cells.

Immunocytochemistry Results: Immunohistochemistry staining patterns were consistent with previous results of studies of pheochromocytoma in various species including humans. The tumors were positive for neuron-specific enolase, S-100 protein, vimentin, and cytokeratin.

Electron Microscopic Findings: The tumor cells contained numerous cytoplasmic neurosecretory granules so called norepinephrine containing eccentrically located electron-dense core surrounded by a wide submembranous space.

Discussion: Pheochromocytoma is a rare chromaffin paraganglioma of the adrenal medulla that typically secretes norepinephrine. Patients with this condition often have paroxysmal or persistent hypertension, headaches and increased levels of catecholemine metabolites. In 1859, Oliver and Shafer demonstrated that adrenal extract raised the blood pressure when injected into experimental animals. In 1902, an active ingredient, epinephrine, was isolated and characterized and, in 1922, a syndrome of paroxysmal hypertension associated with an adrenal medullary tumor, pheochromocytoma was reported.

Hypertension is the major cardiovascular manifestation of pheochromocytoma. Its lability sometimes distinguishes it from other forms of hypertension, and specific laboratory testing permits establishment of the proper diagnosis. The diagnosis of pheochromocytoma is established only by documenting high urinary concentrations of catecholamines or one of their metabolites.

Gross anatomic features including a large tumor involving the right adrenal and invading and causing obstruction of the posterior vena cava are characteristics of the tumor in the dogs, bulls and humans. Histopathologic, immunocytochemical, and electron microscopic findings of this tumor in the ferret are identical to that of dogs and humans with pheochromocytoma.

Cause of sudden death in this ferret is most likely cardiac failure caused by circular myocardial necrosis of the extensively hypertrophied left ventricle. Circular myocardial necrosis in the severely hypertrophied heart of a ferret with pheochromocytoma can be explained by poor collateral flow of the subendocardial myocardium during the physical stress of radiologic examination. These lesions in the ferret are similar to those seen in dogs and humans with concentric hemorrhagic necrosis and in humans with stone heart syndrome.

Cause of left ventricular hypertrophy in this ferret with pheochromocytoma was most likely caused by the tumor secreting and inducing norepinephrine hypertension. Left ventricular hypertrophy is also seen in dogs with pheochromocytoma.

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Comparative Pathology Case 39

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Clinical History: A 35-year-old male patient was noted to have paroxysmal high blood pressure with throbbing headache and cold sweat for 2 years, especially after micturition.

MRI and MIBG nuclear medicine scanning showed a tumor nodule, 3 x 2 x 2 cm. in the anterior urinary bladder wall. Cystoscopic examination revealed a non-papillary and broad based tumor in the anterior wall of bladder. Partial cystectomy was done to excise the tumor smoothly. The patient's headache subsided, and the hypertension was under good control.

Diagnosis: Extra-adrenal Pheochromocytoma (Paraganglioma) of urinary bladder.

Gross Findings: The specimen submitted is a partially resected urinary bladder measuring 4 x 3.3 x 2.3 cm. in size. On cut, there was an ill-defined grayish-brownish solid tumor measuring up to 3 cm. in greatest dimension in the submucosal and muscle layers of bladder wall.

Histopathological Findings: Sections of the bladder wall showed an ill-defined nodule composed of solid nests or acini of polyhedral cells containing purplish granular cytoplasm in a highly vascularized stroma in the smooth muscle layer. Focal cellular areas with nuclear pleomorphism were noted. The resection margins were free of tumor involvement.

Immunohistochemical and Electron Microscopic Studies: Immunostaining showed that the tumor cells were reactive against neuron-specific enolase and synaptophysin antibodies and the sustentacular cells were reactive against S-100 antibody.

Ultrastructural study demonstrates neuroendocrine granules in the cytoplasm of tumor cells.

Discussion: Urinary bladder (extra-adrenal) pheochromocytoma is a catecholamine-producing tumor that arises from chromaffin cells in the extra-adrenal paraganglion system of the urinary bladder. The symptoms and signs result from the release of epinephrine and/or non-epinephrine, which is more prominent during micturition. The most serious consequences of the disease are paroxysmal hypertension during micturition and malignant degeneration. Thus, proper treatment is mandatory.

Pheochromocytoma is known as a rare tumor present in the urinary bladder. Up to 1988, 145 cases had been reported in the literature and 32 cases in mainland China. Most of them were case reports. Micturition difficulties associated with unstable hypertension, tachycardia, and profuse sweating could be a sign of pheochromocytoma of the urinary bladder. Of all pheochromocytomas, 10-36% are located extra-adrenally, in which case they are also referred to as paragangliomas, and 1-3% are found in the urinary bladder.

Diagnosis required not only CT, NMR, excretory urography, and MIBG scintigraphy, but also hormonal analyses. A precise history and careful diagnosis were necessary before a pheochromocytoma of the bladder can be disclosed and treated. Successful treatment of this lesion required a high index of suspicion based upon the patient's symptom complex, allowing preoperative preparation prior to surgical manipulation.

The histologic features of the tumor were characteristic, with pattern virtually indistinguishable from pheochromocytoma of adrenal medulla. It was composed of nests or Zellballen of polygonal cells with round nuclei and abundant granular cytoplasm. The tumor nests were separated by thin fibrovascular septa. Most of the

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tumors were poorly circumscribed and interdigitate with muscle fibers of the bladder wall. Histology revealed malignancy in up to 10 to 20% of the cells; it is thought that focal invasions of tumor into vessels and destruction of connective tissue might be pathognomonic. Malignancy cannot be determined by histological appearance; local invasion of surrounding tissue or distant metastases indicated malignancy.

Ultrastructural study demonstrated neuroendocrine granules in the cytoplasm of tumor cells and immunoreactivity for neuron-specific enolase and synaptophysin. The absence of cytokeratin, and epithelial marker, was a useful feature for distinguishing pheochromocytomas from carcinomas of the bladder.

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Comparative Pathology Case 40

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Clinical History: One eight-month retired female Sprague-Dawley CD (Crl: ^v (SD)BR) rat had axillary enlarged mass.

Diagnosis: Mammary gland fibroadenoma, pericanalicular type, solitary, right thoracic mammary gland.

Gross Findings: Spherical mass, 5 cm in diameter, was noted in the right thoracic axillary subcutaneous area. The mass showed solid, rubbery, firm consistency yellowish-white, granular fibrous-like appearances.

Histopathological Findings: Microscopic Examination of the mammary tissue revealed this is a fibroadenoma consisted of multiple, well circumscribed subcutaneous nodule with capsules formed by proliferative compressed surrounding connective tissues. The nodule was primarily out growth of the ductal epithelium accompanied by overgrowth of connective tissues which grew around and infiltrating into the proliferative tubular glandular structures. The ducts were lined with single to triple layer of cuboidal, uniform epithelial cells. The surrounding connective tissues were loose, with moderately amount of matured uniform fibroblasts. The tubular epithelial cells were cuboidal, with distinct cell border; moderate amount of eosinophilic cytoplasm; small, round to ovoid, central-located nuclei, vesicular chromatin and single small nucleoli. Mitotic figures were rare.

Electron Microscopic Findings: Processing

Microbiological Results: This rat was free of antibody titers to the following viruses: PVM, Reo-3, Sendai, LCM, GD-VII, MVM, MAD, H-1, KRV, RCV, Mycoplasma pulmonis, and pathogenic microorganisms-Corynebacterium kutscheri, Bordetella bronchiseptica, Salmonella spp., Yersinia pseudotuberculosis.

Discussion: Mammary tumors are relatively common occurrence in older female rats, particularly the Sprague-Dawley (SD) rats. The majority of mammary tumors (approximately 85-90%) are the benign fibroadenoma, and most of the remainder are categorized as carcinomas.

Mammary neoplasms in the rat are classified into a variety of morphologic schemes, but most fall within the general categories of fibroadenoma, adenoma, adenocarcinoma, and carcinosarcoma (mixed).

Fibroadenoma in the rat is a circumscribed mass composed of glandular and fibrous components. These firm, white, often large, lobular benign neoplasms have highly variable composition with the two elements present in varying amounts from a neoplasm much like an adenoma to ones in which rare epithelial clusters are present and the mass resembles fibroma. The epithelial component resembles normal acini with epithelial cells arranged in clusters or groups of alveol of fairly uniform cells with little if any mitotic activity. Some ductular structures are lined by a single layer of cuboidal to columnar cells.

Fibroadenoma is the most common benign tumor of the female breast. These tumors occur at any age within the reproductive period of life, more common before age 30. They vary in size from under 1 cm to giant form 10 to 15 cm in diameter. The histologic pattern are usually divided into pericanalicular, intracanalicular fibroadenoma, tubular adenoma as well as lactating adenoma. In rats, the first type is the most common and the other three are rarely seen.

Diagnostic Criteria:

1. Composed of glandular epithelium and fibrous connective tissue.
2. Epithelium is generally single layered and uniform and may contain lipid vacuoles.
3. Connective tissue distributed within and between lobules ranges from well-differentiated to dense hyalinized collagen with few interspersed fibrocytes.
4. Epithelium often forms ductules, alveoli, or small cysts vacuoles.
5. Focal areas of atypia and/or cellular pleomorphism may be present.
6. Mast cells may be frequent.

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Comparative Pathology Case 41

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Clinical History: A 17-year-old unmarried female presented a movable tumor mass, 1x1x0.8 cm, in right breast for 2 months. She received excisional biopsy.

Diagnosis: Fibroadenoma.

Gross Findings: A round, rubbery, firm mass has well-circumscribed outline and appears white, solid and bulging on sections.

Histopathological Findings: The microscopic appearance shows a sharply-demarcated lesion in which there is proliferation of both stromal and epithelial components. The stroma consists of fibroblastic proliferation with interspersed collagen and rare mitoses. The epithelial components are tubules or ducts that are composed of cuboidal or low columnar cells with round uniform nuclei resting on a myoepithelial cell layer. Some ducts are distorted and elongated and compressed slit-like structures, resulting in a so-called intracanalicular pattern. In other areas, round or oval ducts not compressed by the proliferating connective tissue produce a pericanalicular growth pattern.

Discussion: Fibroadenomas are the most common breast tumor in adolescent and young adult women, with a peak age incidence in the third decade. The tumors present as well-circumscribed, freely movable, nonpainful masses. It increases in size during pregnancy and tends to regress as the age of the patient increases. The tumors are most often solitary; however, as many as 25% of cases have multiple lesions in one or both breasts or they develop subsequent tumors.

Fibroadenomas arise from the ducts and stroma of the terminal part of the mammary duct system and can be characterized as a giant lobule formed by exaggerated and uncoordinated epithelial and stromal growth.

Morphologic variations in fibroadenoma are plentiful, some of more significance than others. Fibrocystic changes are evident in approximately 50% of fibroadenomas. These may consist of apocrine metaplasia, which is found in about 15% of the cases, adenosis, or intraductal hyperplasia. Sclerosing adenosis occurs in less than 10% of fibroadenomas and may result in a pattern that simulates invasive carcinoma, especially on frozen sections. The presence of spindled myoepithelial cells in adenosis is a helpful diagnostic findings. Intraductal hyperplasia in a fibroadenoma does not appear to be associated with an increased risk for subsequent carcinoma.

Squamous metaplasia is a rare findings; its presence in abundance should suggest the alternative possibility of phylloids tumor. Lactational changes are manifested by an increase in the amount of cytoplasm in the epithelial cells, which appear vacuolated, and by dilatation of the glandular lumina by secretion. Infarction in the absence of pregnancy is rare and recognition of such foci is important to prevent confusion with necrotic carcinoma. There may be variable stromal cellularity, ranging from hypercellularity to hypocellularity. Atrophic ducts, and hyalinization, calcification, and ossification of the stroma are more commonly seen in aged patients or longstanding tumors. Rarely, otherwise characteristic fibroadenomas may contain multinucleated giant cells, bundles of smooth muscle cells, mature adipose tissue, metaplastic cartilage, or prominent myxoid changes. Fibroadenomas should be distinguished from other fibroepithelial neoplasms including sclerosing lobular hyperplasia, juvenile fibroadenoma and phylloides tumor. Malignant change in fibroadenoma are found on only 0.1% of the cases. They usually involve the epithelial component. The mean age of patients with carcinoma occurring in a fibroadenoma is approximately two decades older than the average age of patients with fibroadenomas.

In cases of fibroadenomas containing carcinoma, 95% of the cases were in situ lesions. Lobular carcinoma in situ is much more common than intraductal carcinoma.

Fibroadenomas may be excised with narrow margins of normal tissue. There is no evidence of an increase risk of malignant change to cystosarcoma.

Treatment of fibroadenoms containing carcinoma depends upon the type and extent of carcinoma and should be the same as for patients with comparable lesions not affecting a fibroadenoma.

Diagnostic Criteria:

1. Round, white, firm, solid mass, usually no more than 3 cm in diameter.
2. Proliferation of both loose connective tissue stroma and epithelial tubules lined by two cell types.

Reference:

1. Paul Peter Rosen and Harold A. Oberman, Tumors of the Mammary Gland, Atlas of Tumor Pathology, Third Series, Fascicle 7, AFIP, 1993.

Comparative Pathology Case 42

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Clinical History: The patient was a 6 years old pointer bitch, body weight 13.4 kg. The owner said, a hard mass was palpated near the left second to third mammary glands about one and a half year ago. The mass enlarged during last 3 weeks. The bitch had good spirit and appetite till now.

Physical examination revealed a hard rock like mass, about 13 x 9 x 4.5 cm in size, under subcutis in the left second to third mammary glands. Left axillary lymph node was swelling to 3.5 x 3 x 2 cm. X-ray of the chest showed a large ellipsoidal smooth edge mass in the subcutis.

The mass in mammary gland and left axillary lymph node were excised by surgeon on 2/8/1996. The bitch showed good health now.

Diagnosis: Canine benign mixed type mammary gland tumor

Gross Findings: The hard mass in the mammary gland was excised with left second nipple and some skin. The mass was well encapsulated by a layer of white tissue under the subcutis, did not involve the skin and nipple.

The cut surface of the mass revealed many small cysts with fluid and yellowish to white round nodules packed together. Yellowish nodules were softer than the white ones, and the later seemed like cartilage.

Histopathological Findings: The section of the encapsulated hard mass from the mammary gland consisted of :1. Lobular adenomatous mammary gland epithelia were papillary, piled up, folding and secretion. The morphology of the adenomatous epithelia were single layer to pseudostratify, cuboidal to tall columnal, pink stain

cytoplasm, nucleus pale stain and markable nucleolus 2. The adenomatous acini contain protein-like substance, necrotic cellular debris and some inflammatory cells. 3. Some myoepithelial and fibrocytic stromas infiltrated with some lymphocytes and macrophages which contain brownish pigment in cytoplasm. 4. Hyaline cartilage or colorless to basophilic stain mucine like ground substance formed round nests surrounded by adenoid to fibrotic cells. 5. Myoepithelial cells showed transtion to tissue that cannot be distinguished from true hyaline cartilage.

The section from the axillary lymph node without the evidence of metastasis from mammary gland tumor.

Discussion: The most common tumor in the female dog is of mammary gland origin. Likewise in this species, malignant mammary gland tumors are by far the leading form of cancer. The approximate median age of dogs with mammary tumors is 10 to 11 years. The reported ages range from 2 to 20 years; however, mammary neoplasia in bitches less than 5 years old is extremely uncommon. About 65% of mammary tumors in dog are benign mixed tumors and 25% are carcinomas; the rest are hyperplasias, adenomas, malignant mixed tumors, and myoepitheliomas. These figures vary considerably because of different methods of classifying the tumors, especially the separation of mixed tumor from carcinoma.

Mixed tumors are derived from more than a single germ layer or more than one derivative of a single germ layer. They are called "mixed" because of the complexity of cellular units that include epithelium, myoepithelium, hyaline cartilage and bone (osteoid and osseous). Stromal fibrosis, when present, is often confused with myoepithelial proliferation.

DIFFERENT MORPHOLOGIC FORMS OF CANINE MAMMARY TUMORS

Benign Mammary tumors	Malignant Mammary Tumors
Benign mixed tumor	Tubular adenocarcinoma
Complex adenoma	Simple and complex types
Fibroadenoma	Papillary adenocarcinoma
Intracanalicular type	Simple and complex types
Pericanalicular type	Papillary cystic adenocarcinoma
Duct papilloma	Simple and complex types
Simple adenoma	Solid carcinoma
	Simple and complex types
	Anaplastic carcinoma
	Other carcinomas
	Mucinous, squamous cell, spindle cell
	Sarcomas
	Osteosarcoma, fibrosarcoma, and combined forms
	Malignant mixed tumor (carcinosarcoma)

Based on the International Histological Classification of Tumors of Domestic Animals published by the World Health Organization, 1974. Modified from Theilen and Madewell: Veterinary Cancer Medicine. Philadelphia, Lea & Febiger, 1979, pp 192-203

CLINICAL STAGING SYSTEM FOR CANINE MAMMARY TUMORS

Stage Grouping	T	N	M
I	T ₁	N ₀ (-) or any N ₂ (-)	M ₀
II	T ₀	N ₁ (+)	M ₀
	T ₁	N ₁ (+)	M ₀
	T ₂	N ₀ (+) or N ₁ a(+)	M ₀
III	T ₃	Any N	M ₀
	Any T	Any N _b	M ₀
IV	Any T	Any N	M ₁

Modified from Owen, L. N., ed.: The TNM Classification of Tumours in Domestic Animals. Geneva: World Health Organization, 1980.

KEY: T (Primary Tumor): T₀= no evidence of tumor; T₁= tumor less than 1 cm maximum diameter; T₂= tumor 1 to 3 cm maximum diameter; T₃= tumor more than 3 cm maximum diameter; T₄= tumor any size, inflammatory carcinoma; N(Regional Lymph Nodes[RLN]): N₀= no RLN involved; N₁=ipsilateral RLN involved; N₂= bilateral RLN involved; a= not fixed; b= fixed; - = histologically negative; + = histologically positive; M(Distant Metastasis); M₀= no evidence of distant metastasis; M₁= distant metastasis

Diagnostic Criteria:

1. Adenoma and hyaline cartilage in the same tumor mass.
2. Axillary lymph node without tumor cell metastasis.

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Comparative Pathology Case 43

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Clinical History: A 31 y/o female had a nodular mass over upper medial aspect of right breast noted two years ago. She received excisional biopsy at Lin Hospital, Chia-yi County and pathologically benign was told. But another nodular mass over peripheral region of the original mass was noted three months later. In October 1995, she received excisional biopsy again and early malignancy was found. Then she visited our OPD and received simple mastectomy with adjuvant chemotherapy.

Diagnosis: Phyllodes tumor, malignant.

Gross Findings: The breast tissue from simple mastectomy is 600 gm and 15x12x7 cm. The overlying 10x7.5 cm fusiform skin has an unremarkable nipple at its center. A 13x11x6.5 cm well circumscribed mass is gray brown to yellow and soft to firm in consistency. The cut surface shows cleft-like appearance.

Microscopic Findings: The sections of the breast mass show lobulated, cleft-like spaces scattered within an overgrow stroma. The stroma has prominent spindle cells with apparent nuclear atypia, hyperchromatism, and mitoses. The mitotic rate is up to 3-4 per high- power field with an average about 5/10HPF. Some mitoses are atypical ones. There is no necrosis, cystic degeneration or hemorrhage found.

Discussion: Phyllodes tumors of the breast are fibroepithelial tumors composed of an epithelial and a cellular stromal component. The average annual age-adjusted incidence of phyllodes tumor is 2.1 per 1 million women. The peak age is 45-49 y/o. Asian and Latin patients are significantly younger.

Grossly, typical phyllodes tumors are round, relatively well circumscribed and firm. The cut surface is solid, homogeneous gray white with multiple cleft-like spaces. Areas of necrosis, cystic degeneration, and hemorrhage may be present.

Microscopically, the two key features of phyllodes tumor are stromal hypercellularity and the presence of benign glandular elements as an integral component of the neoplasm. Phyllodes tumor is a spectrum of disease and classified as benign, borderline, and malignant arbitrarily. Although a sharp distinction between benign and malignant forms of phyllodes tumor is not always possible, some criteria are used clinically. These criteria are tumor margin, stromal cellularity, nuclear pleomorphism, and mitotic figure. Cytologically, malignant phyllodes tumors have marked nuclear atypia, numerous mitoses, and loss of the relationship between stroma and glands.

Ultrastructurally, features of the tumor cells are largely those of fibroblasts with occasional muscle differentiation.

Treatment of phyllodes tumor is determined by histological configuration. Local excision with wide safe margin is the treatment of choice for benign phyllodes tumor. Simple mastectomy is sufficient for most cytologically malignant phyllodes tumors. There is no need for removal of axillary lymph nodes, except for the exceptional instance which they are clinically involved.

No single criterion can accurately predict the prognosis of phyllodes tumor. The DNA ploidy and whether there is tumor necrosis or not may have some value for assessment of the prognosis.

Diagnostic Criteria:

1. Cleft-like cut surface with pushing or infiltrating tumor margin.
2. Overgrowth of stroma, normal epithelial glands, with loss of relationship of these two components.
3. Chaotic stroma with marked nuclear atypia, hyperchromatism, prominent mitoses, occasionally atypical, and necrosis.

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Comparative Pathology Case44

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Clinical History: An 8-month-old, male, mongrel dog was brought to National Taiwan University Veterinary Hospital (NTUVH) for the presence of numerous wart-like mucosal growths in the oral cavity.

Diagnosis: Canine oral papilloma, compatible with papillomavirus infection.

Gross Findings: Several pieces of masses were submitted for pathological examination. The size of the masses was varied. The large ones had the cauliflower-like appearance, typical of papillomas, with 8-10 mm in diameter.

Histopathological Findings: The masses consisted of papillomatous proliferation of thickened squamous epithelium occasionally enclosing a thin core of propria papillae. The stratum spinosum was thickened and the cells were swollen with vesiculation in both cytoplasm and nucleus. Hypergranulosis with cytoplasmic vacuolation and prominent keratohyaline granules were also evident in stratum granulosum. Occasionally, a vague eosinophilic nuclear inclusion was noted in the distended granulosous cells.

Discussion: Base on the history, clinical signs, gross and microscopical features of the masses, canine oral papilloma has been diagnosed. Attempt to pursuit the possible viral infection of this case by electromicroscopic examination and polymerase chain reaction is undergoing.

Oral papilloma of the dogs has been associated with viral infection. True oral papilloma is very rare. The tumor mainly affects pups (average age of 1 year). There are usually multiple growths and are often occurred on buccal mucosa, tongue, plate, pharynx, and epiglottis. The cause of the disease is papillomavirus which is the member of Papovavirade. The virus shows strong tissue and host specificity. The tumor is contagious. The episode of the tumor usually lasts for several weeks to months and is followed by spontaneous regression. Regression has been related to the formation of host cellular immunity.

Infection is established in the basal layer of squamous epithelium with low level of viral DNA replication. Maturation of the viral replication is following the differentiation of the epithelium. Intact viral particles can be seen in the stratum granulosum and reach peak in the stratum corneum which facilitate its transmission of the disease.

Most papillomaviruses cause benign tumor in mucosal or cutaneous area in domestic animals . However, in associated with certain cofactors, bovine, human and rabbit papillomaviruses may produce malignant tumors.

In our case, an autogenic vaccine has been administered. In less than two weeks, complete regression was noted after the vaccination. The efficacy of this treatment will be discussed.

Diagnostic Criteria:

1. Clinical history, demonstration of characteristic lesions with or without intranuclear viral inclusion bodies.
2. Electromicroscopical examination or polymerase chain reaction.

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Comparative Pathology Case 45

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Clinical History: A 47-year-old man suffered for a white patch over Left buccal mucosa for about 2 years. Except foreign body sensation, there was nothing particular. And the patient had betel nut chewing habit for over 10 years.

Physical examination revealed a papillomatous elevated white mass (size: 1.5 x 2 cm) over Left buccal mucosa near 678 area(fig 1).

Diagnosis: Squamous cell papilloma

Gross Findings: The lesion is an exophytic growth made up of numerous, small finger-like projections which result in a lesion with a roughened, verrucous or cauliflower-like surface. It was nearly a well circumscribed sessile mass, which present homogenous white color and measured about 1.5 x 2 cm (fig 2).

Histopathological Findings: The microscopic appearance was characteristic and consisted of many papillary projections extending above the surface of the mucosa (fig 3). These extension epithelium were supported by a well-vascularized connective tissue stroma. Except acanthosis, a high-magnification revealed parakeratin layer on the epithelial surface. Mitosis and koilocytosis may be found. A distinct maturational sequence could be noted, and there is no significant sign of dysplasia or atypism. Epithelium and underlying lamina propria were edematous and contained severe infiltration of chronic inflammatory cells (fig 4).

Treatment: Excision

Discussion: The papilloma is the most common benign neoplastic lesion of oral mucosa and makes up approximately 2.5% of oral lesions. They may be found on the vermilion portion of the lips and any intraoral mucosal site, with predilection on the tongue, palate and uvula and can occur at any age. The lesion shows a range of size and shapes and their color varies depending on the degree of surface keratinization from pink to white. Most present clinically as single lesion; however, multiple lesions occasionally occur. And the lesions are generally asymptomatic. The etiology of oral papilloma is obscure. Viral infection, endocrine and mechanical stimulation, especially dental cause are putative etiologic agents. Surgical removal is the treatment of choice by either routine excision or laser ablation. Recurrence is uncommon, and the malignant degeneration is also quite unlikely.

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