Connective tissue lesions

Reactive hyperplasias

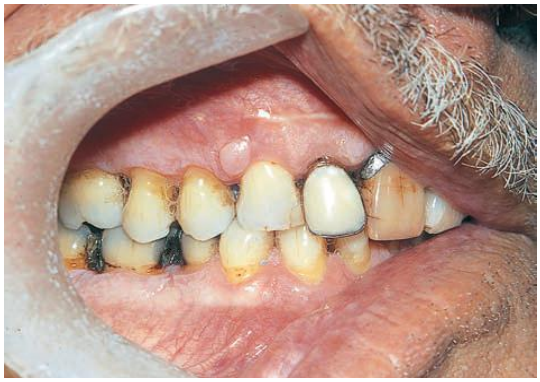
Reactive hyperplasias comprise a group of fibrous connective tissue lesions that commonly occur in oral mucosa secondary to injury. They represent a chronic process in which exuberant repair (granulation tissue and scar) follows injury. As a group, these conditions present as submucosal masses that may become secondarily ulcerated when traumatized such as during mastication. Their color ranges from lighter than the surrounding tissue (because of a relative reduction in vascularity and increase in collagen) to red (because of an abundance of well-vascularized granulation tissue). Because nerve tissue does not proliferate with reactive hyperplastic tissue, these lesions are painless. The reason for the exuberant repair is unknown. Treatment generally consists of surgical excision and removal of the irritating factor(s).

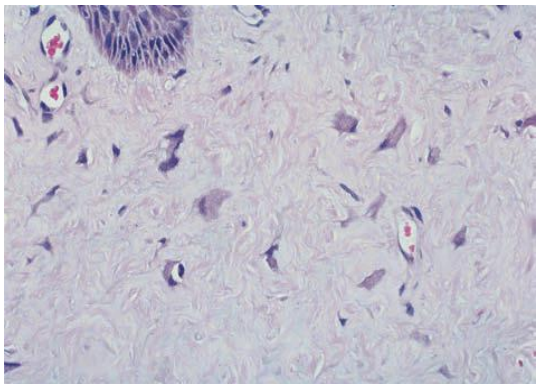
Peripheral Fibroma

Peripheral fibroma is a reactive hyperplastic mass that occurs on the gingiva and is believed to be derived from connective tissue of the submucosa or periodontal ligament. It may present clinically as a stalked (pedunculated) or a broad-based (sessile) mass that is similar in color to surrounding connective tissue. Ulceration may be present over the summit of the lesion. It rarely causes erosion of subjacent alveolar bone.

Histopathology

Peripheral fibroma is a form of fibrous hyperplasia that may also be called hyperplastic scar. It is highly collagenous and relatively avascular, and it may contain a mild to moderate chronic inflammatory cell infiltrate. This lesion is basically the gingival counterpart to traumatic fibroma occurring in other mucosal regions. Microscopically, several subtypes (below) of this lesion have been identified (Peripheral ossifying fibroma, Peripheral odontogenic fibroma, Giant cell fibroma)





Treatment: by local excision, which should include the periodontal ligament, if involved.

Focal Fibrous Hyperplasia

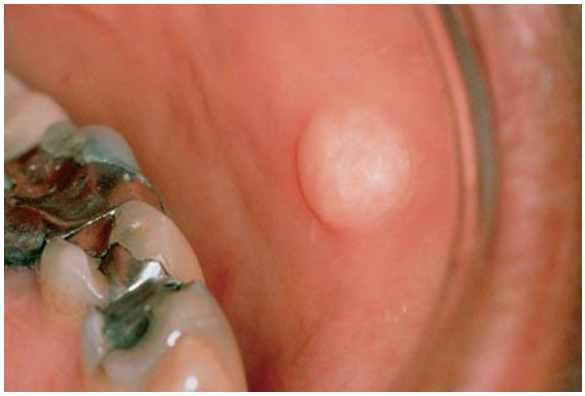
Focal fibrous hyperplasia is a reactive lesion usually caused by chronic trauma to oral mucous membranes. Overexuberant fibrous connective tissue repair results in a clinically evident submucosal mass.

Clinical Features

Focal fibrous hyperplasia is typically found in frequently traumatized areas, such as the buccal mucosa, the lateral border of the tongue, and the lower lip. It is a painless, broad-based swelling that is paler in color than the surrounding tissue because of its relative lack of vascular channels. The surface may occasionally be traumatically ulcerated, particularly in larger lesions. Lesions have limited growth potential and do not exceed 1 to 2 cm in diameter.

Histopathology

Collagen overproduction is the basic process that dominates the microscopy of this lesion. Fibroblasts are mature and widely scattered in a dense collagen matrix. Sparse chronic inflammatory cells may be seen, usually in a perivascular distribution. Overlying epithelium is often hyperkeratotic because of chronic low-grade friction.



Focal fibrous hyperplasia

Oral Fibrous Hyperplasia synonyms

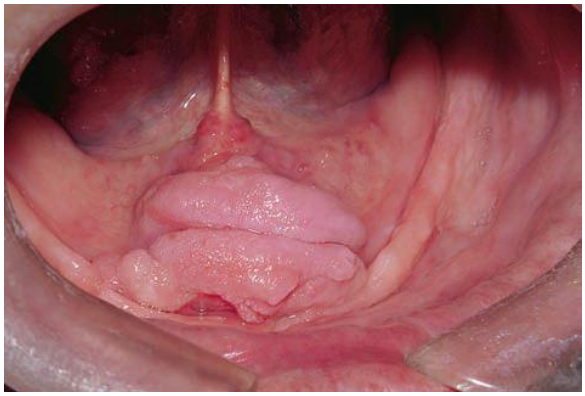
(Traumatic fibroma, Irritation fibroma, Hyperplastic scar, Inflammatory fibrous hyperplasia, Peripheral fibroma of gingiva, Fibrous epulis of gingiva, Denture induced fibrous hyperplasia, Epulis fissuratum)

Denture-Induced Fibrous Hyperplasia

Denture-induced fibrous hyperplasia of oral mucosa is related to the chronic trauma produced by an ill-fitting denture.

Clinical Features

Denture-induced fibrous hyperplasia is a common lesion that occurs in the vestibular mucosa and less commonly along the mandibular lingual sulcus where the denture flange contacts tissue. As the bony ridges of the mandible and the maxilla resorb with long term denture use, the flanges gradually extend farther into the vestibule. There, chronic irritation and trauma may incite an exuberant fibrous connective tissue reparative response. The result is the appearance of painless folds of fibrous tissue surrounding the overextended denture flange.



Denture-induced fibrous hyperplasia

Myxoma

Myxoma is a soft tissue neoplasm composed of gelatinous material resembling fetal umbilical cord and a myxoid microscopic appearance. The oral form of soft tissue myxoma is a rare lesion that presents as a slow-growing, asymptomatic submucosal mass, usually in the palate.

Histopathology

Oral myxomas are not encapsulated and may exhibit infiltration into surrounding soft tissue. Dispersed stellate and spindle shaped fibroblasts are found in a loose myxoid stroma.

Treatment by surgical excision

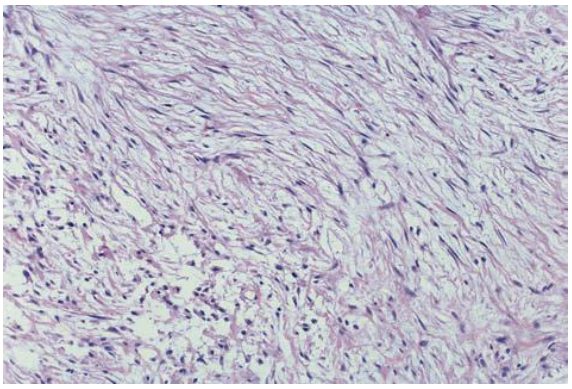
Nodular Fasciitis

Nodular fasciitis (pseudosarcomatous fasciitis) represent benign proliferation of myofibroblast cell. The exact cause is unknown. It is now thought to be a clonal neoplasm. The condition typically presents as a firm mass in the dermis or the submucosa and exhibits rapid growth. Pain or tenderness often accompany the process. Intraorally, the buccal mucosa is the most commonly affected site. Nodular Fasciitis often managed by excision

to remove the growing mass and to confirm the diagnosis. If left untreated, regression will occur.

Histopathology

A nodular growth contains plump spindle cells with vesicular nuclei in a (haphazard to storiform arrangement). Myxoid areas are usually found. Multinucleated giant cells are occasionally present and may originate from adjacent muscle or from fusion of macrophages. Mitotic figures may be frequent but are morphologically normal in appearance. Inflammatory cells and extravasated red blood cells are also microscopic features of nodular fasciitis.



Treatment

Conservative surgical excision is the treatment of choice for nodular fasciitis. Local recurrence occurs in only 2% of cases.

Fibromatosis

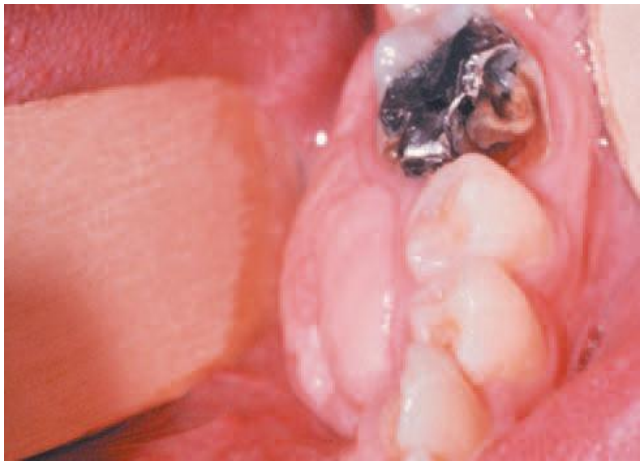
Fibromatosis comprises a group of locally aggressive neoplasms that show infiltrative, destructive, and recurrent growth but no tendency to metastasize. They are classified as superficial (palmar, plantar) or deep (desmoid). Superficial fibromatoses do not occur in the oral cavity.

Deep fibromatoses are clinically diverse, deep-seated, fibrous proliferations. Three types have been identified:

- Sporadic
- familial adenomatous polyposis (FAP) associated
- multicentric (familial).

Clinical Features

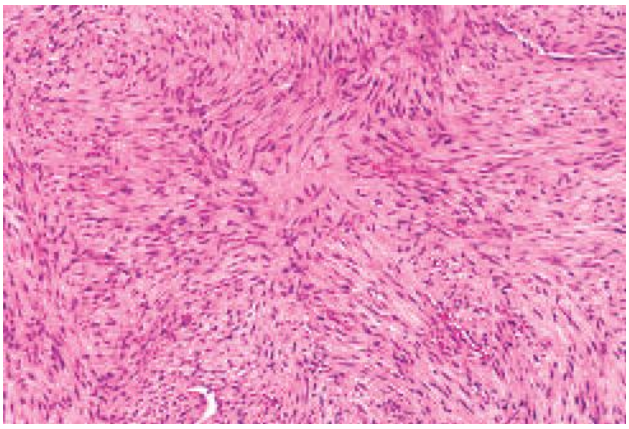
Soft tissue fibromatosis of the head and neck is a fi rm, painless mass, which may exhibit rapid or insidious growth. The lesion most frequently occurs in children or young adults; hence, the term juvenile fibromatosis. The most common oral site is the para-mandibular soft tissue region, although the lesion can occur almost anywhere. The tumor can grow to considerable size, resulting in significant facial disfigurement. Destruction of adjacent bone may be observed on radiographs and other imaging studies.



Histopathological features

Fibromatosis is an unencapsulated infiltrative lesion with a fascicular growth pattern. The lesion is composed of highly differentiated connective tissue containing uniform, compact fibroblasts, often surrounded by abundant collagen. Nuclei are not atypical, and mitotic

figures are infrequent. When muscle invasion occurs, giant cells representing degenerate muscle cells may be seen. Slit-like vascular spaces are usually seen as well. Overall, the bland microscopic appearance of this lesion belies its locally aggressive behavior.

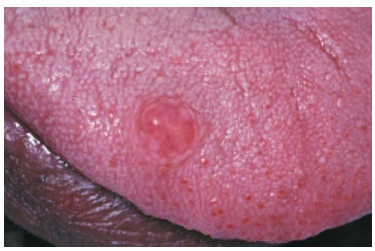


Treatment

Because of its locally aggressive nature, the preferred treatment for soft tissue fibromatosis is wide excision that includes a generous margin of adjacent normal tissues. Adjuvant chemotherapy or radiation therapy sometimes has been used for incompletely resected or recurrent tumors. A 23% recurrence rate has been reported for oral and para-oral fibromatosis.

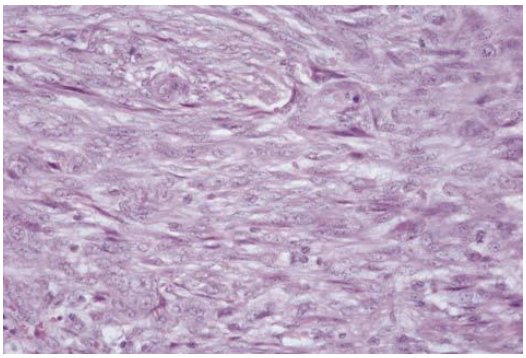
Benign Fibrous Histiocytoma

Benign fibrous histiocytomas are rare fibroblastic neoplasms. These are adult lesions, typically noted in the fifth decade and present as painless masses that may be ulcerated. Intrabony lesions present as radiolucencies, often with ill-defined margins.



Histopathological features

This tumor is fairly well demarcated and often is circumscribed at the periphery. A storiform (cartwheel or matlike) growth pattern of spindle cells (fibroblasts) is noted, with plump or vesicular nuclei admixed with some inflammatory cells. Tumor giant cells may be seen. No cellular atypia is present, and mitotic figures are infrequent and normal in appearance.



Treatment: Local surgical excision is the treatment of choice. Recurrence is uncommon,

Fibrosarcoma

Fibrosarcoma is defined as a rare malignant spindle cell tumor showing a herringbone or interlacing fascicular pattern. The cause of fibrosarcoma is unknown. No specific predisposing factors are known, although some lesions arise in previously irradiated sites, and others are noted in preexisting connective tissue tumors such as solitary fibrous tumor, well-differentiated liposarcoma, and dermatofibrosarcoma.

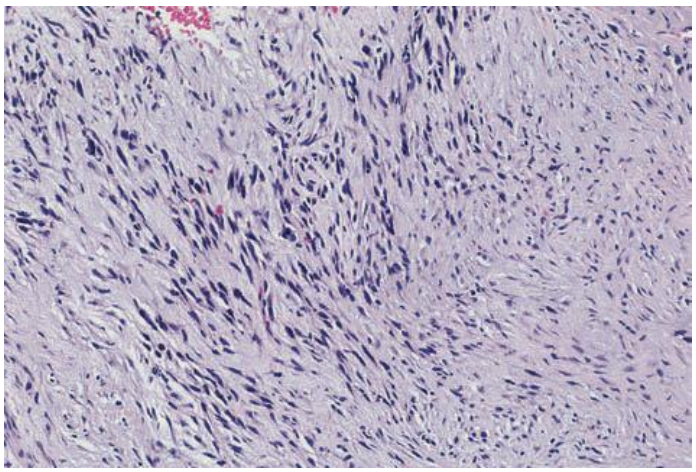
Clinical features

Fibrosarcoma is a rare soft tissue and bony malignancy of the head and neck. A tumor results from proliferation of malignant mesenchymal cells at the site of origin. Secondary ulceration may be seen as the lesion enlarges. Young adults are most commonly affected.

This is an infiltrative neoplasm that is more of a locally destructive problem than a metastatic problem.

Histopathology

Microscopically, fibrosarcoma exhibits malignant-appearing fibroblasts, typically in a herringbone or interlacing fascicular pattern. Collagen may be sparse, and mitotic figures frequent. The degree of cell differentiation from one tumor to another may be quite variable. The periphery of this lesion is ill defined because the neoplasm freely invades surrounding tissue. Fibrosarcoma is essentially a diagnosis of exclusion, and by definition, there should be no expression of actin, S-100, epithelial membrane antigen, keratin, CD34, or myogenin.



Fibrosarcoma composed of atypical spindle cells.

Treatment

Wide surgical excision is generally advocated for fibrosarcoma because of the difficulty involved in controlling local growth. Although recurrence is not uncommon, metastasis is infrequent. Fibrosarcomas of bone are more likely to metastasize via the bloodstream than are soft tissue lesions. The overall 5-year survival rate ranges between 30% and 50%. well-differentiated lesions have a better prognosis than do those with poorly differentiated features.

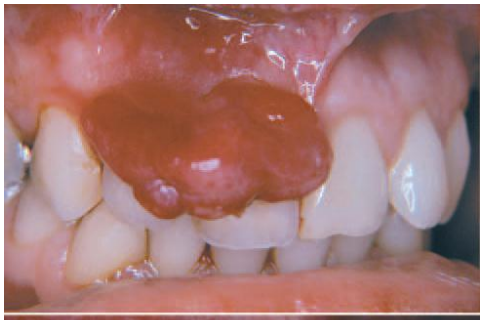
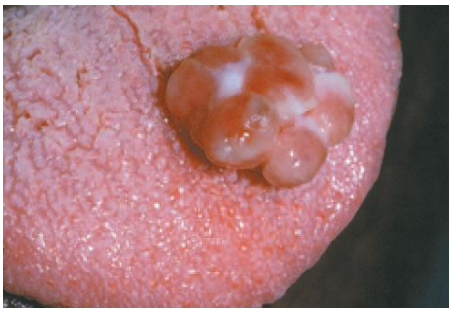
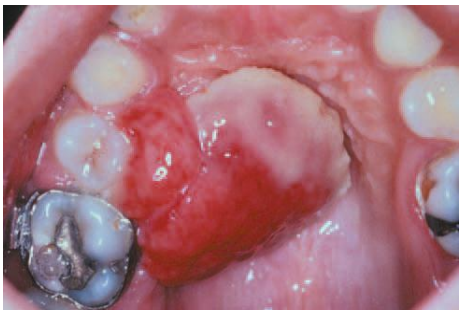
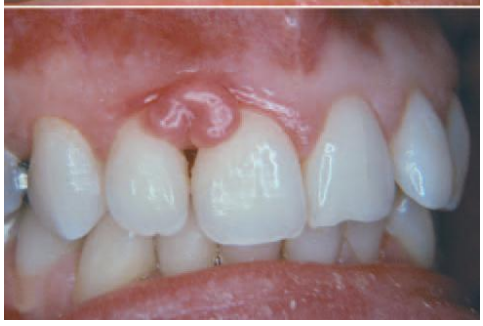
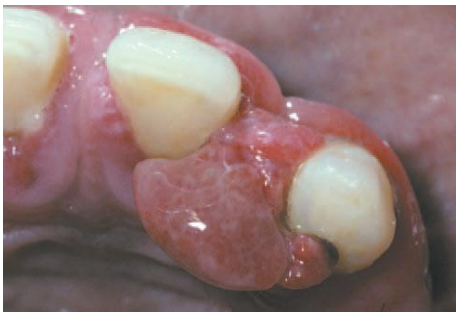
Pyogenic granuloma

The pyogenic granuloma is a common tumorlike growth of the oral cavity believed to be unrelated to infection but represent an exuberant tissue response to local irritation or trauma. In spite of its name, it is not a true granuloma.

Clinical features

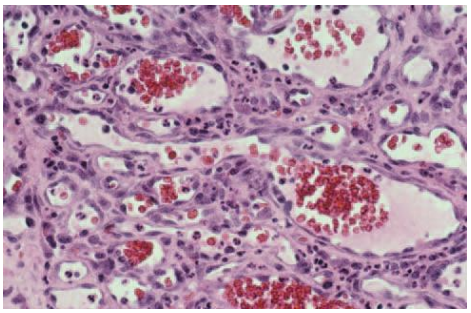
Pyogenic granuloma is a smooth or lobulated mass that is usually pedunculated, although some lesions are sessile. The surface is characteristically ulcerated and ranges from pink to red to purple, depending on the age of the lesion. Young pyogenic granulomas are highly vascular in appearance; older lesions tend to become more collagenized and pink. They vary from small growths only a few millimeters in size to larger lesions that may measure several centimeters in diameter. Typically, the mass is painless, although it often bleeds easily because of its extreme vascularity. Pyogenic granulomas may exhibit rapid growth. Oral pyogenic granulomas show a striking predilection for the gingiva, which accounts for 75% of all cases. Gingival irritation and inflammation that result from poor oral hygiene may be a precipitating factor in many patients. The lips, tongue, and buccal mucosa are the next most common sites. Pyogenic granulomas of the gingiva frequently develop in pregnant women, so much so that the terms *pregnancy tumor or granuloma gravidarum*. Such lesions may begin to develop during the first trimester, and their incidence increases up through the seventh month of pregnancy. The gradual rise in development of these lesions throughout pregnancy may be related to the increasing levels of estrogen and progesterone as the pregnancy progresses. After pregnancy and the return of normal hormone levels, some of these pyogenic granulomas resolve without treatment or undergo fibrous maturation and resemble a fibroma. **Epulis granulomatosa** is a hyperplastic growths of granulation tissue that sometimes arise in healing extraction sockets. These

lesions resemble pyogenic granulomas and usually represent a granulation tissue reaction to bony sequestra in the socket.

Histopathological features

Pyogenic granuloma appears as highly vascular proliferation that resembles granulation tissue. Numerous small and larger endothelium-lined channels are formed that are engorged with red blood cells. These vessels sometimes are organized in lobular aggregates, and some pathologists require this lobular arrangement for the diagnosis (lobular capillary hemangioma). The surface is usually ulcerated and replaced by a thick fibrinopurulent membrane. A mixed inflammatory cell infiltrate of neutrophils, plasma cells, and lymphocytes can be seen. Older lesions may have areas with a more fibrous appearance. In fact, many gingival fibromas probably represent pyogenic granulomas that have undergone fibrous maturation.



The treatment of patients with pyogenic granuloma consists of conservative surgical excision.

Vascular lesions

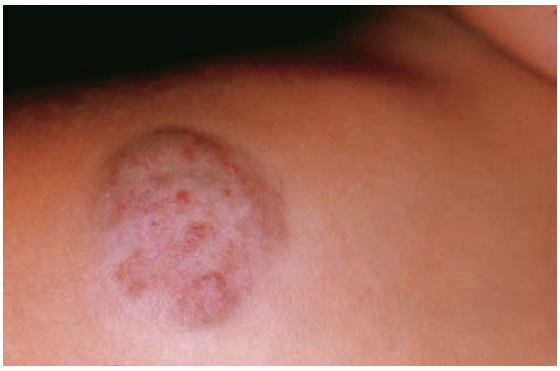
Hemangioma and vascular malformations

Hemangiomas are benign tumors of infancy that display a rapid growth phase with endothelial cell proliferation, followed by gradual involution. Most hemangiomas cannot be recognized at birth, but arise subsequently during the first 8 weeks of life.

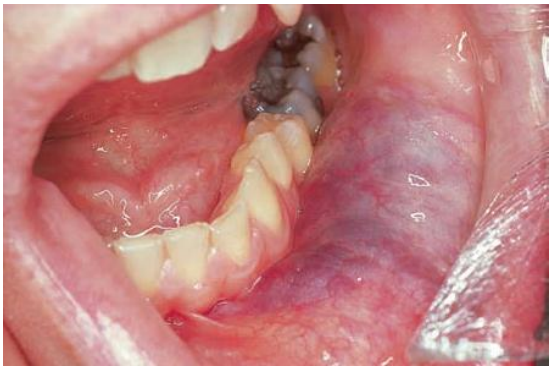
Vascular malformation are structural anomalies of blood vessels without endothelial proliferation. By definition, vascular malformations are present at birth and persist throughout life. They can be categorized according to the type of vessel involved (capillary, venous, arteriovenous) and according to hemodynamic features (low flow or high flow).

	Hemangioma	Vascular Malformation
Description	Abnormal endothelial cell proliferation	Abnormal blood vessel development
Elements	Results in increased number of capillaries	A mix of arteries, veins, and capillaries (includes AV shunt)
Growth	Rapid congenital growth	Grows with patient
Boundaries	Often circumscribed; rarely affects bone	Poorly circumscribed; may affect bone
Thrill and bruit	No associated thrill or bruit	May produce thrill and bruit
Involution	Usually undergoes spontaneous involution	Does not involute
Resection	Persistent lesions resectable	Difficult to resect; surgical hemorrhage
Recurrence	Recurrence uncommon	Recurrence common

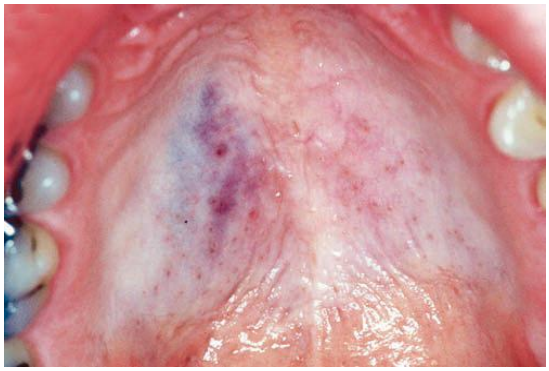
AV, Arteriovenous.



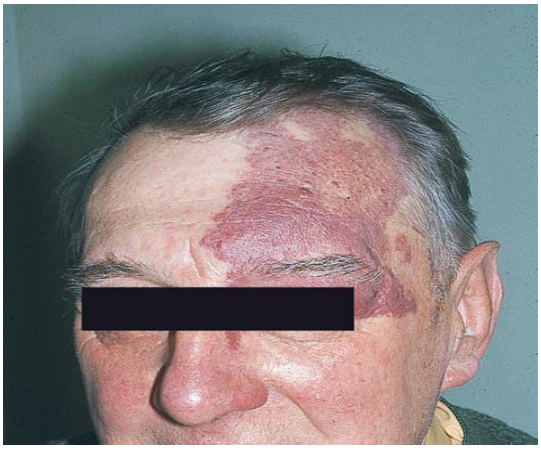
hemangioma



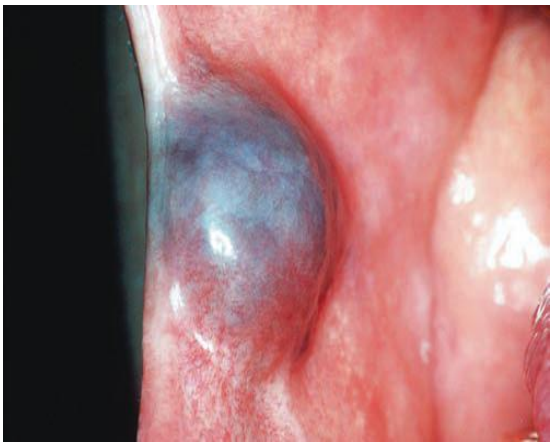
Vascular malformation of lip



Vascular malformation of palate



Vascular malformation in Sturge-Weber syndrome



vascular malformation of buccal mucosa

Histopathology

Congenital hemangiomas are composed of abundant capillary spaces lined by endothelium without muscular support. Congenital vascular malformations may consist not only of capillaries, but also of venous, arteriolar, and lymphatic channels. Direct arteriovenous communications are typical. Lesions may be of purely one type of vessel, or they may consist of two or more vessels. Vascular morphology accounts for lesions exhibiting rapid flow versus those exhibiting slow flow.

Treatment

Spontaneous involution during early childhood is likely for congenital hemangiomas. If these lesions persist into the later years of childhood, involution is improbable and definitive treatment may be required. Good results may be achieved with propranolol, a nonselective beta-adrenergic blocking agent. Congenital vascular malformations generally do not involute, and they may require surgical intervention if eradication is the goal. Adjuncts include selective arterial embolization and sclerosant therapy. Laser therapy is another accepted form of primary treatment of selected vascular lesions. Because the margins of these lesions are often ill defined, total elimination may not be practical or possible.

Encephalotrigeminal Angiomatosis (Sturge-Weber Syndrome)

Encephalotrigeminal angiomatosis, or Sturge-Weber syndrome, is a non-inherited neurocutaneous syndrome that includes vascular malformations with characteristic distribution. Venous malformations involve the leptomeninges of the cerebral cortex, usually with similar vascular malformations of the face. The associated facial lesion, also known as port-wine stain or **nevus flammeus**, involves the skin innervated by one or more branches of the trigeminal nerve. Port-wine stains may also occur as isolated lesions of the skin without the other stigmata of encephalotrigeminal angiomatosis. The vascular defect

of encephalotrigeminal angiomatosis may extend intraorally to involve the buccal mucosa and the gingiva. Ocular lesions (vascular malformations, glaucoma) may appear. Neurologic effects of encephalotrigeminal angiomatosis may include mental retardation, hemiparesis, and seizure disorders.

Lymphangioma

Lymphangiomas are benign, hamartomatous tumors of lymphatic vessels. They are not true neoplasms; instead, they most likely represent developmental malformations that arise from sequestrations of lymphatic tissue that do not communicate normally with the rest of the lymphatic system.

There are three types of lymphangioma:

1. Lymphangioma simplex (capillary lymphangioma), which consists of small, capillary-sized vessels.

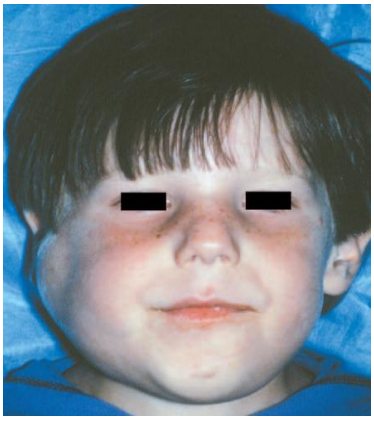
2. Cavernous lymphangioma, which is composed of larger, dilated lymphatic vessels.

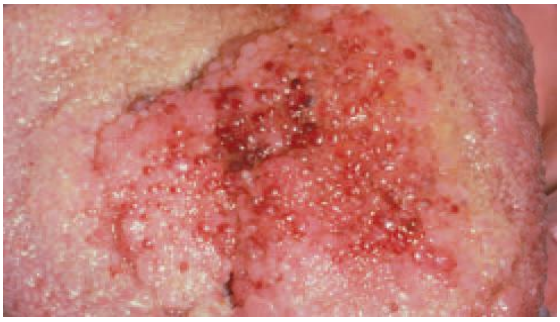
3. Cystic lymphangioma (cystic hygroma), which exhibits large, macroscopic cystic spaces.

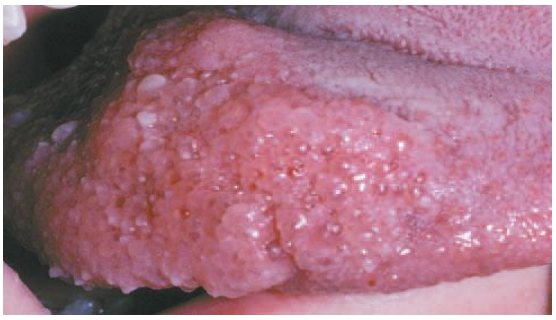
Clinical features

Lymphangiomas have a marked predilection for the head and neck. About half of all lesions are noted at birth, and around 90% develop by 2 years of age. Cervical lymphangiomas are more common in the posterior triangle and are typically soft, fluctuant masses. They occur less frequently in the anterior triangle (lesions in this location are more likely to result in respiratory difficulties or dysphagia if they grow large). Cervical lymphangiomas may extend into the mediastinum or upward into the oral cavity. Such tumors can become massive and can measure 15 cm or greater in size. Rapid tumor enlargement may occur

secondary to an upper respiratory tract infection, presumably because of increased lymph production, blocked lymphatic drainage, or secondary infection of the tumor. Oral lymphangiomas may occur at various sites but are most frequent on the anterior two thirds of the tongue, where they often result in macroglossia. the tumor is superficial in location and demonstrates a pebbly surface that resembles a cluster of translucent vesicles.



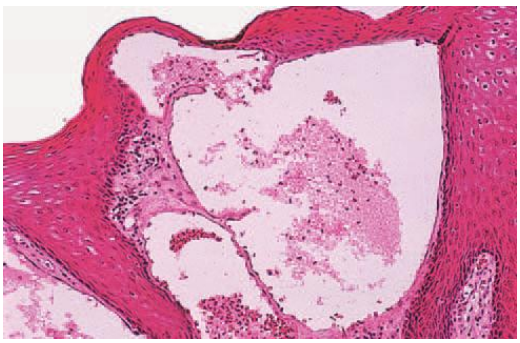




lymphangioma.

Histopathological features

Lymphangiomas are composed of lymphatic vessels that may show marked dilatation (cavernous lymphangioma) or macroscopic cyst-like structures (cystic hygroma). The vessels often diffusely infiltrate the adjacent soft tissues and may demonstrate lymphoid aggregates in their walls. The lining endothelium is typically thin, and the spaces contain proteinaceous fluid and occasional lymphocytes. Some channels also may contain red blood cells, which creates uncertainty as to whether they are lymphatic or blood vessels.



Cavernous lymphangioma

Treatment

The treatment of lymphangiomas usually consists of surgical excision, although total removal may not be possible in all cases because of large size or involvement of vital structures. Recurrence is common, especially for cavernous lymphangiomas of the oral cavity, because of their infiltrative nature.

Angiosarcoma

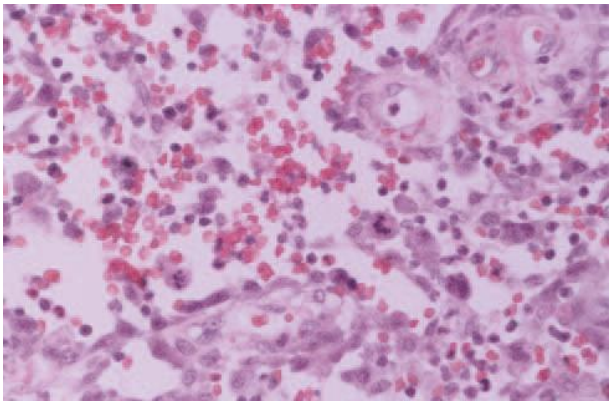
Angiosarcoma is a rare malignancy of vascular endothelium, which may arise from either blood or lymphatic vessels. More than 50% of all cases occur in the head and neck region, with the scalp and forehead being the most common sites. Oral lesions are quite rare. The term **hemangioendothelioma** is used to describe vascular tumors with microscopic features intermediate between those of hemangiomas and angiosarcomas. Such tumors also are rare and are considered to be of intermediate malignancy.

Clinical features

Oral angiosarcomas have been reported in various locations; the tongue and mandible are two of the more common sites.

Histopathological features

Angiosarcoma is characterized by an infiltrative proliferation of endothelium-lined blood vessels that form an anastomosing network. The endothelial cells appear hyperchromatic and atypical; they often tend to pile up within the vascular lumina. Increased mitotic activity may be seen. Immunohistochemical studies show the tumor cells to be positive for CD31 and factor VIII–related antigen in most cases, whereas CD34 positivity is observed less consistently.



Angiosarcoma. Sinusoidal vascular spaces lined by pleomorphic endothelial cells.

Treatment

Treatment usually consists of radical surgical excision, radiation therapy, or both. The prognosis for angiosarcoma of the face and scalp is poor, with a reported 10- year survival rate of only 21%. However, angiosarcomas of the oral cavity and salivary glands appear to have a better outcome.

Kaposi's sarcoma

Kaposi's sarcoma is an unusual vascular neoplasm that was first described in 1872 by Moritz Kaposi, a Hungarian dermatologist. Before the advent of the acquired immunodeficiency syndrome (AIDS), it was a rare tumor. In early 1980s, Kaposi's sarcoma became quite common because of its propensity to develop in individuals infected by the human immunodeficiency virus (HIV). Since the introduction of highly active

antiretroviral therapy (HAART) in the mid- to late 1990s, the prevalence of AIDS-related Kaposi's sarcoma in the Western world has declined. Evidences suggest that Kaposi's sarcoma is caused by human herpesvirus 8 (HHV-8; Kaposi's sarcoma–associated herpesvirus [KSHV]). Kaposi's sarcoma is a multifocal neoplasm of vascular endothelial cell origin that was described initially in patients over the age of 60. The lesion most likely arises from endothelial cells, with some evidence of lymphatic origin. Four clinical presentations are recognized:

1. Classic

2. Endemic (African)

3. Iatrogenic immunosuppression associated

4. AIDS related

- Classic (chronic) Kaposi's sarcoma is primarily a disease of late adult life, and 70% to 90% of cases occur in men. It mostly affects individuals of Italian, Jewish, or Slavic ancestry. Multiple slowly growing (over years) blue-purple macules and plaques are present on the skin of the lower extremities Oral lesions are rare and most frequently involve the palate.
- Endemic type

  Endemic Kaposi's sarcoma in Africa has been divided into four subtypes:

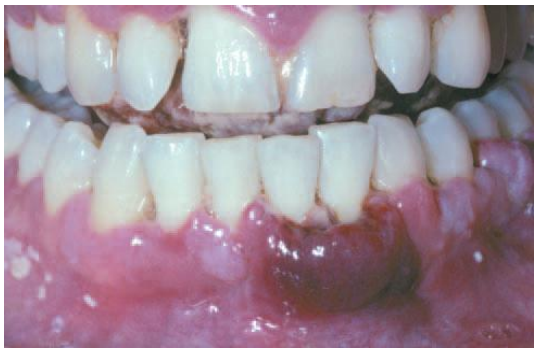
  1. A benign nodular type, similar to classic Kaposi's sarcoma

  2. An aggressive or infiltrative type, characterized by progressive development of locally invasive lesions that involve the underlying soft tissues and bone

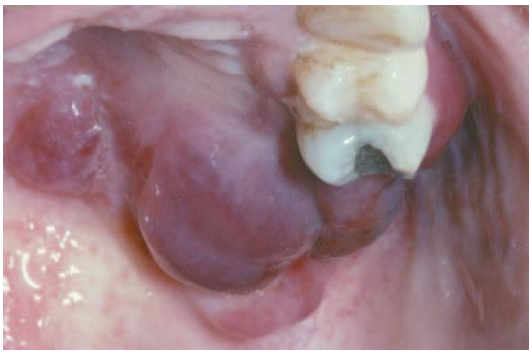
  3. A florid form, characterized by rapidly progressive and widely disseminated, aggressive lesions with frequent visceral involvement

4. A unique lymphadenopathic type, occurring primarily in young black children and exhibiting generalized, rapidly growing tumors of the lymph nodes, occasional visceral organ lesions, and sparse skin involvement.

- Iatrogenic type: Iatrogenic immunosuppression-associated Kaposi's sarcoma most often occurs in recipients of organ transplants.
- AIDS related: KS typically manifests as multiple lesions of the skin or oral mucosa. The trunk, arms, head, and neck are the most commonly involved anatomic sites. Approximately 70% of individuals with HIV-related KS of skin or viscera demonstrate oral lesions; which may be the initial manifestation. Hard palate, gingiva, and tongue are affected most frequently. When present on the palate or gingiva, the neoplasm can invade bone and create tooth mobility. The lesions begin as brown or reddish-purple macular lesions that do not blanch with pressure. With time, the macules typically develop into plaques or nodules. Pain, bleeding, and necrosis may become a problem and necessitate therapy.



HIV-associated Kaposi's sarcoma
Raised, dark-red enlargement of gingiva



HIV-associated Kaposi's sarcoma
Diffuse, red-blue nodular enlargement of the left hard palate

Histopathological features:

Kaposi's sarcoma typically evolves through three stages:

1. **Patch (macular):** characterized by proliferation of miniature vessels resulting in an irregular, jagged vascular network that surrounds preexisting vessels.

2. **Plaque:** further proliferation of these vascular channels along with the development of a significant spindle cell component.

3. **Nodular:** The spindle cells increase to form a nodular tumorlike mass that may resemble a fibrosarcoma or other spindle cell sarcomas. Numerous extravasated erythrocytes are present, and slit-like vascular spaces may be distinguished.

Treatment and prognosis

The treatment of Kaposi's sarcoma depends on the clinical subtype and stage of the disease. radiotherapy, surgical excision, systemic chemotherapy may be used. Intralesional injection of chemotherapeutic agents is used to control individual lesions. Mean survival time is 10 to 15 years.