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Tumor Markers in Common Oral and Maxillofacial Lesions

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Additional information is available at the end of the chapter

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1. Introduction

Immunohistochemical (ihc) stains are widely used for diagnosis of tumors. In this chapter we present modern immunohistochemical stains for diagnosing those tumors that cannot be evaluated via common or routine stains such as hematoxylin and eosin.

2. Epithelial tumors

Squamous cell carcinoma (SCC) and malignant melanoma are common epithelial lesions that require IHC.

2.1. Squamous cell carcinoma

2.1.1. Definition

SCC is a malignant neoplasm arising from the squamous epithelium of the oral cavity most commonly from the lip, then tongue, floor of mouth, gingiva, palate, and buccal mucosa. Premalignant changes present as white (leukoplakia) or red (erythroplakia) mucosal patches.

2.1.2. Immunohistochemical stains

Squamous carcinomas are nearly always positive for CK.

- Common CK expression in squamous carcinomas includes AE1/AE3 and CKs 5, 5/6, 14, and 17.

- Nuclear p63 expression is common in squamous cell carcinomas but is not specific
- Cytokeratin stains may help detect subtle metastatic foci especially in post-treatment lymph nodes (Figure 1).
- Over expression of p53 may be linked to response to radiation and/or chemotherapy
- p16 positive: strong and diffuse nuclear and cytoplasmic expression in oropharyngeal carcinoma (HPV associated). [1-5]

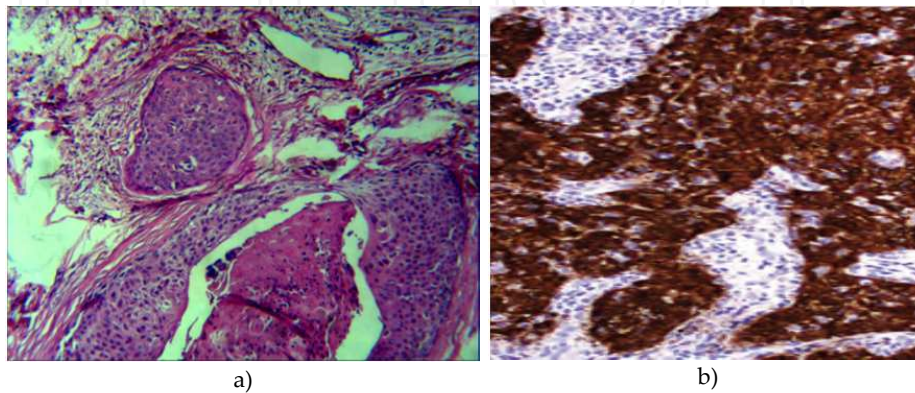


Figure 1. a) Squamous cell carcinoma (H&E). b) Cytokeratin stains in SCC.

2.2. Mucosal melanoma

2.2.1. Definition

Malignant mucosal melanoma (MMM) is a neural crest–derived neoplasm originating from melanocytes and demonstrating melanocytic differentiation.

2.2.2. Immunohistochemical stains

S100 protein, Melan A, HMB45, tyrosinase, vimentin are positive, Keratin and muscle markers are negative (Figure 2). [6-13]

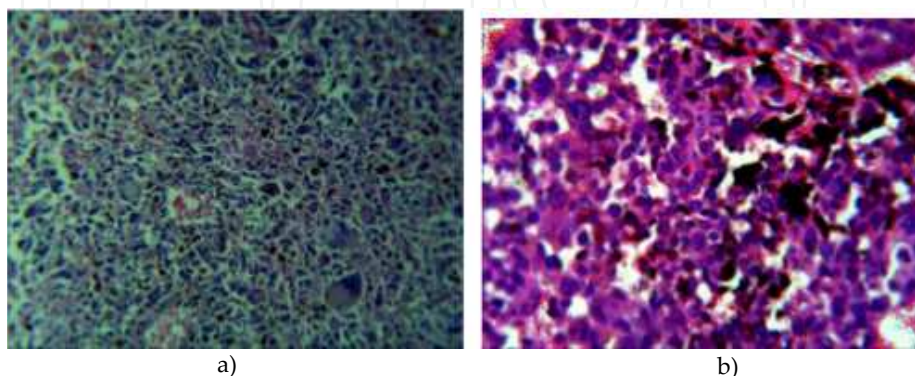


Figure 2. a) Mucosal melanoma (H&E) b) IHC staining for HMB-45

3. Salivary gland tumors

The common salivary gland tumors needing IHC are:

- PLEOMORPHIC ADENOMA
- BASAL CELL ADENOMA
- CANALICULAR ADENOMA
- ONCOCYTOMA
- PAPILLARY CYSTADENOMA LYMPHOMATOSUM (WARTHIN TUMOR)
- SEBACEOUS ADENOMA/LYMPHADENOMA
- MUCOEPIDERMOID CARCINOMA
- ADENOID CYSTIC CARCINOMA
- POLYMORPHOUS LOW-GRADE ADENOCARCINOMA
- EPITHELIAL-MYOEPITHELIAL CARCINOMA
- CLEAR CELL CARCINOMA
- ACINIC CELL CARCINOMA

3.1. Pleomorphic adenoma

3.1.1. Definition

A benign neoplasm composed of ductal epithelial and myoepithelial cells set within a mesenchymal stroma.

3.1.2. Immunohistochemical stains

Cytokeratin cocktail, S100 protein, SMA, p63, calponin, MSA, GFAP, and CD10 reactive the cells are highlighted by a mixture of epithelial and myoepithelial markers that include AE1/AE3, CK5/6, CK7, and CK14; S-100 protein; p63; SMA; calponin; and GFAP. (Figure 3). [14-16]

3.2. Basal cell adenoma

3.2.1. Definition

Basal cell adenoma is a benign salivary gland epithelial neoplasm composed of a proliferation of small basaloid cells in solid, tubular, trabecular, or membranous patterns. (Figure 4).

3.2.2. Immunohistochemical stains

Immunohistochemical Inner luminal cells: cytokeratin cocktail, CK7, and CD117 Peripheral basaloid cells: S100 protein, p63, SMA, and MSA [17 -19]

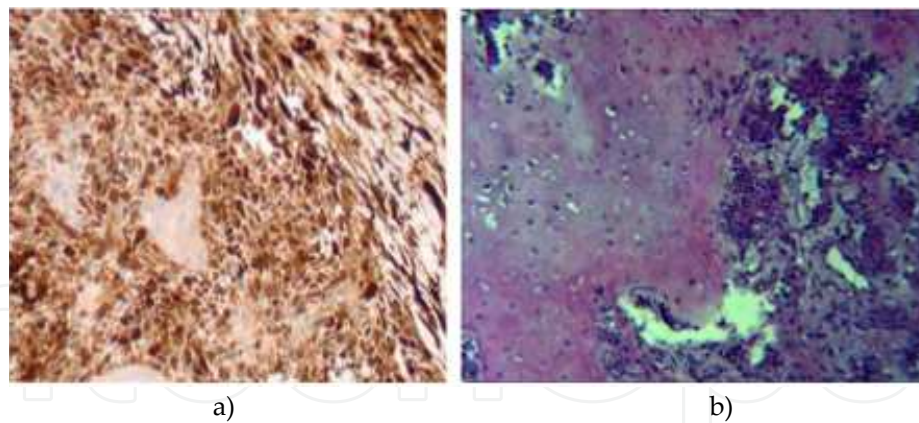


Figure 3. a) Pleomorphic adenoma shows a mixture of myoepithelial cells and isolated duct-tubular structures b) S-100 protein in the myoepithelial cells.

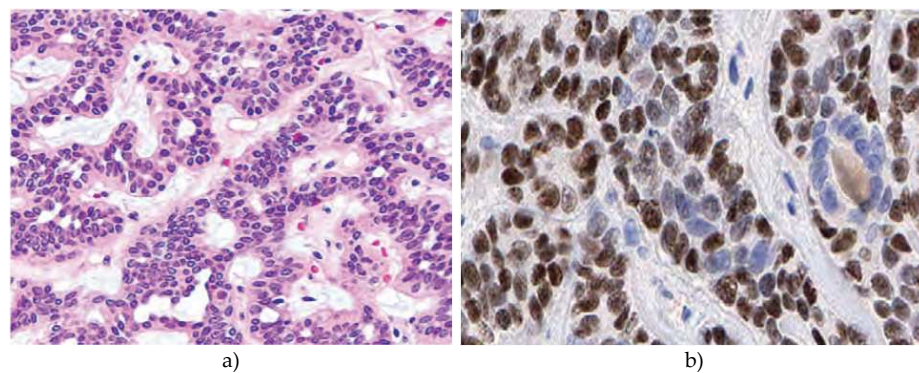


Figure 4. a) Basal cell adenoma, trabecular type b) p63 highlights the basal cells

3.3. Canalicular adenoma

3.3.1. Definition

Canalicular adenoma is a benign epithelial salivary gland neoplasm characterized by chains of columnar cells and preference for the minor salivary glands.

3.3.2. Immunohistochemical stains

Cytokeratin and S100 protein reactive GFAP is reactive at the tumor/connective tissue interface (Figure 5.) [17-23].

3.4. Oncocytoma

3.4.1. Definition

Oncocytoma (oncocytic adenoma) is a putative neoplastic proliferation of oncocytically altered cells.

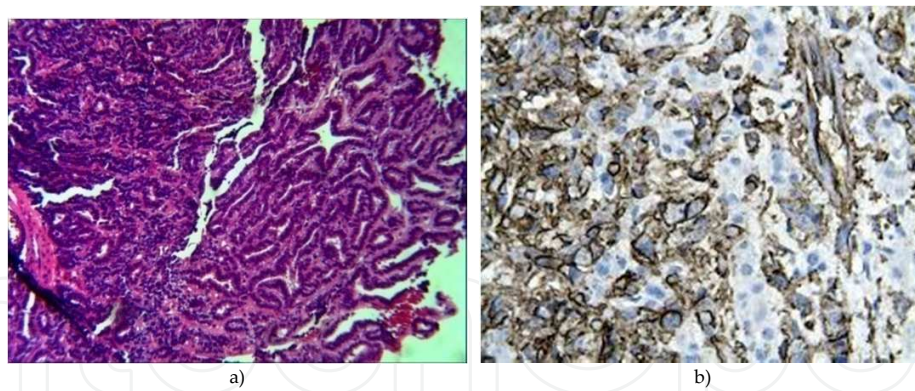


Figure 5. a) Canalicular adenoma, b) GFAP staining is positive

3.4.2. Immunohistochemical stains)

Cytokeratin, p63, and PTAH reactive (Figure 6) [17- 19, 21, 22]

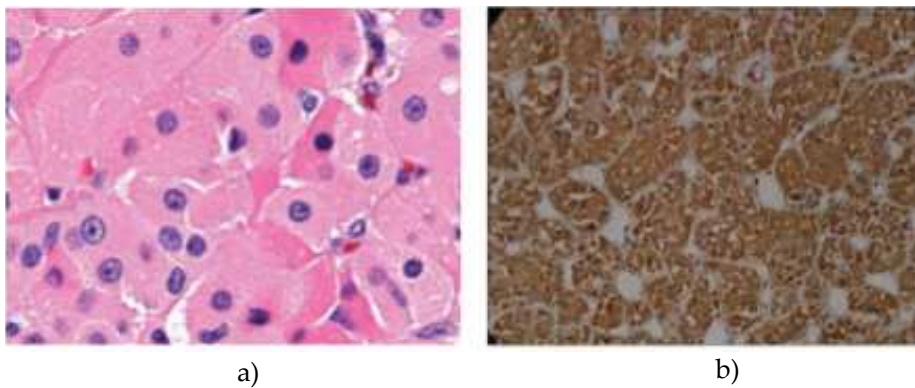


Figure 6. a) Oncocytes are Cytokeratin, highly positive polygonal cells with abundant granular eosinophilic cytoplasm and round, centrally placed nuclei, with or without nucleoli. b) p63 reactive.

3.5. Papillary cystadenoma lymphomatosum (Warthin's tumor)

3.5.1. Definition

Warthin's tumor is a relatively common lesion composed of a double layer of oncocytic and cystic architectural pattern cells, and a dense lymphoid epithelium in a papillary stroma. (Figure7)

3.5.2. Immunohistochemical stains

Epithelial component keratin reactive Lymphoid component reactive with B- and T-cell markers [17- 19]

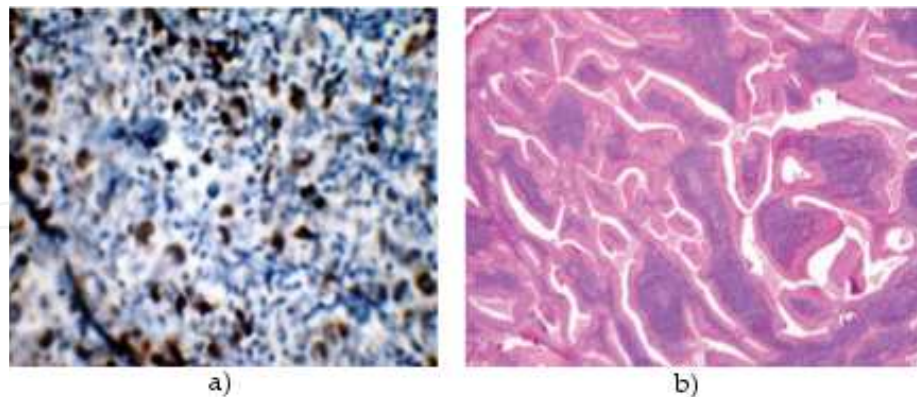


Figure 7. a) Papillary-cystic tumor associated with a dense lymphoid stroma. b) KI 67 positive B- cell component.

3.6. Sebaceous adenoma / lymphadenoma

3.6.1. Definition

Sebaceous adenoma is a benign epithelial neoplasm composed of proliferating, incompletely differentiated sebaceous glands. Sebaceous lymph adenoma is a rare variant in which the epithelial proliferation is supported by a dense lymphoid stroma and possibly arises from entrapped salivary gland tissue within intraparotid or periparotid lymph nodes (Figure 8).

3.6.2. Immunohistochemical stains

Immunohistochemistry can be used to confirm the sebaceous differentiation (such as with CD15, androgen receptor, or EMA Epithelial component is cytokeratin and is EMA reactive) [17-19]

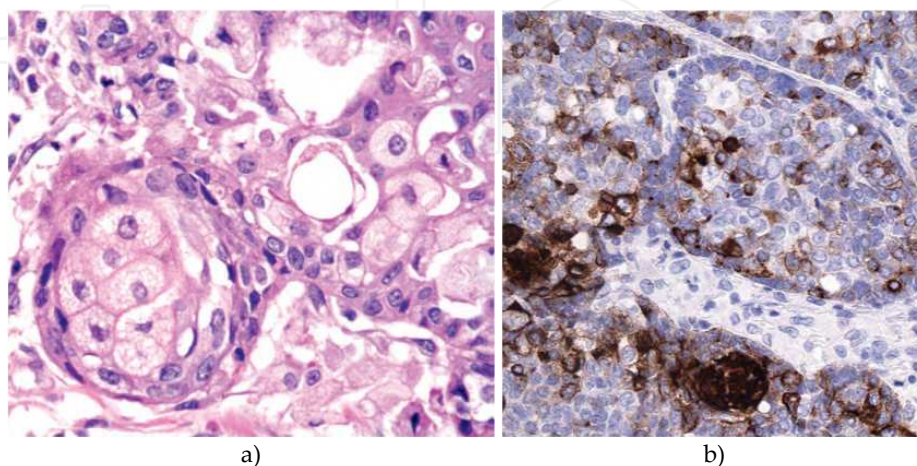


Figure 8. a) Sebaceous lymphadenoma b) EMA highlights the sebocytes

3.7. Mucoepidermoid carcinoma

3.7.1. Definition

A malignant glandular epithelial neoplasm characterized by mucus, intermediate, and epidermoid cells. This common salivary gland malignancy represents between 2% and 16% of all salivary gland tumors and up to one third of malignant salivary gland tumors.

3.8. Immunohistochemical stains

Intermediate and epidermoid cells are immunoreactive for cytokeratin and frequently EMA. Three cell populations can generally be seen in MEC- epidermoid cells, mucous cells, and intermediate cells— variably set within a cystic background (Figure 9).

CK5/6, Ki-67, and p63 nuclear expression may help in the differential diagnosis. [23, 24]

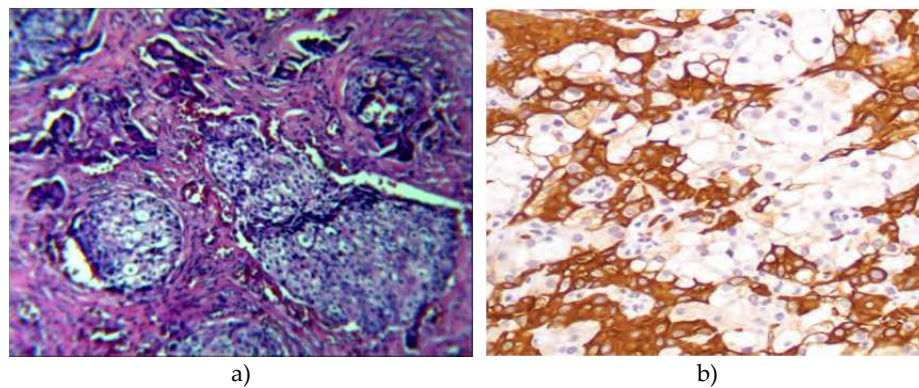


Figure 9. a) Mucoepidermoid carcinoma(H&E) and b) CK5/6 highlight the epidermoid and intermediate cells.

3.9. Adenoid cystic carcinoma

3.9.1. Definition

Adenoid cystic carcinoma accounts for 10% of all malignant salivary gland tumors. ACC is cribriform and has two prominent growth patterns: Tubular, and solid, and it is composed of epithelial and myoepithelial cells (Figure 10).

3.9.2. Immunohistochemical stains

Pseudocysts are positive for PAS, Alcian blue, laminin, and type IV collagen. Epithelial cells are positive for low-molecular-weight keratins, EMA, and CD117. Myoepithelial cells are positive with calponin, SMA, S100 protein, and p63. [25 – 32].

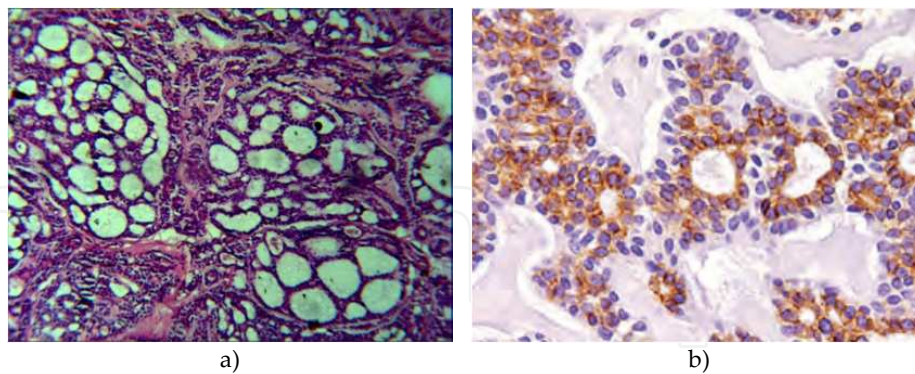


Figure 10. a) Adenoid cystic carcinoma showing multiple patterns b) CD117 highlights the epithelial cells.

Polymorphous low-grade adenocarcinoma.

3.9.3. Definition

This is a malignant epithelial tumor characterized by an infiltrative growth of cytologically uniform cells (“low-grade”) arranged in architecturally diverse patterns (polymorphous), slowly growing tumor that exclusively affects the minor salivary glands, most often of the palate (Figure 11).

3.9.4. Immunohistochemical stains

Cytokeratin, vimentin, and S100 protein are positive. Variable results are seen with immunohistochemistry and are rarely of diagnostic value. It reacts with EMA, S-100 protein, and Bcl-2; these findings can help differentiate it from PA and ACC. [17-19, 33]

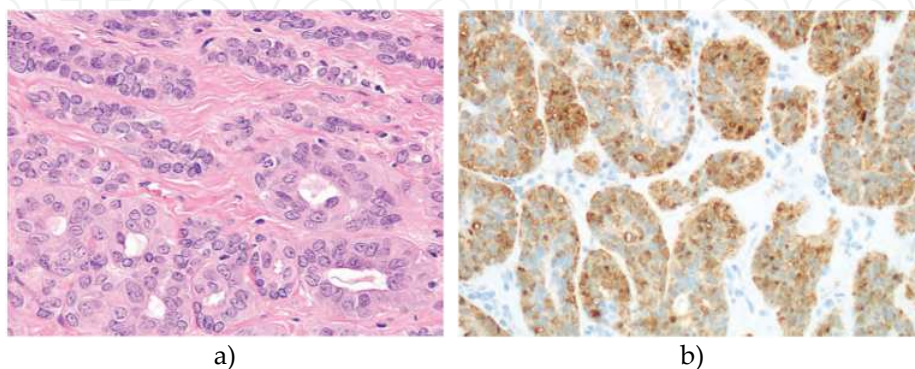


Figure 11. a) polymorphous low-grade adenocarcinoma b) S-100 protein

3.10. Epithelial-myoepithelial carcinoma

3.10.1. Definition

Epithelial-myoepithelial carcinoma is a low-grade, malignant, biphasic salivary tumor that comprises 1% to 2% of all salivary neoplasms, the majority of which develop in the parotid gland. It is a malignant neoplasm with biphasic duct-like structures composed of an inner layer of duct lining, epithelium-type cells and an outer layer of clear, myoepithelial-type cells (Figure 12).

3.10.2. Immunohistochemical stains

Inner cells are positive for keratin; outer myoepithelial cells are calponin, SMA, p63, and, less reliably, S100 protein positive; CD117 and bcl-2 are frequently positive. [17- 19, 34

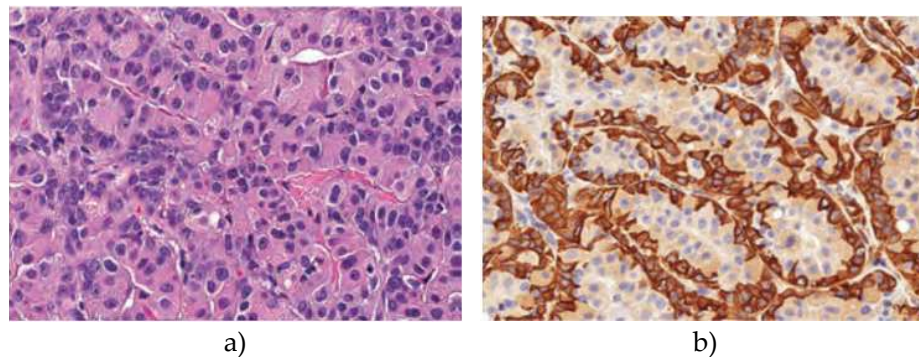


Figure 12. a) Epithelial-myoepithelial carcinoma b) smooth muscle actin strongly stains the myoepithelial cells

3.11. Clear cell Carcinoma

3.11.1. Definition

Many salivary and nonsalivary tumors contain clear cells. Among these are mucoepidermoid carcinoma, acinic cell carcinoma, oncocytoma, renal cell carcinoma, myoepithelioma, and clear cell odontogenic carcinoma.

3.11.2. Immunohistochemical stains

The neoplastic cells are positive with AE1/AE3, CAM5. 2, CK7, EMA, and p63; cells are negative with S-100 protein, calponin, actins, and GFAP (Figure 13). They are usually negative for myoepithelial markers that include S-100 protein, MSA, SMA, SMMHC, calponin, and GFAP and are also negative for CD10, CK20, vimentin, desmin, RCC, CA9, and Pax-2 see). [35-37]

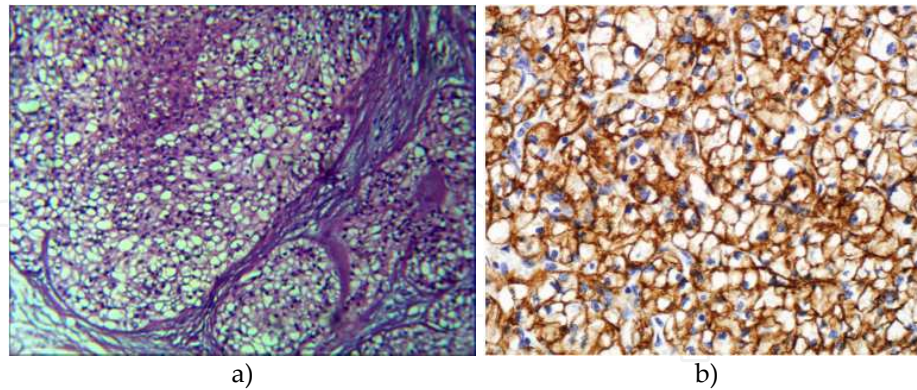


Figure 13. a) Clear cell carcinoma b) Highlighted clear cells by S100

3.12. Acinic cell carcinoma

3.12.1. Definition

A malignant epithelial neoplasm demonstrating serous acinar cell differentiation with cytoplasmic zymogen secretory granules (Figure 14).

3.12.2. Immunohistochemical stains

PAS-positive, diastase-resistant zymogen granules. Acinic cells may stain positively for amylase, transferrin, lactoferrin, CEA, VIP, and others. About 10% show some positivity for S100 protein. [38, 39]

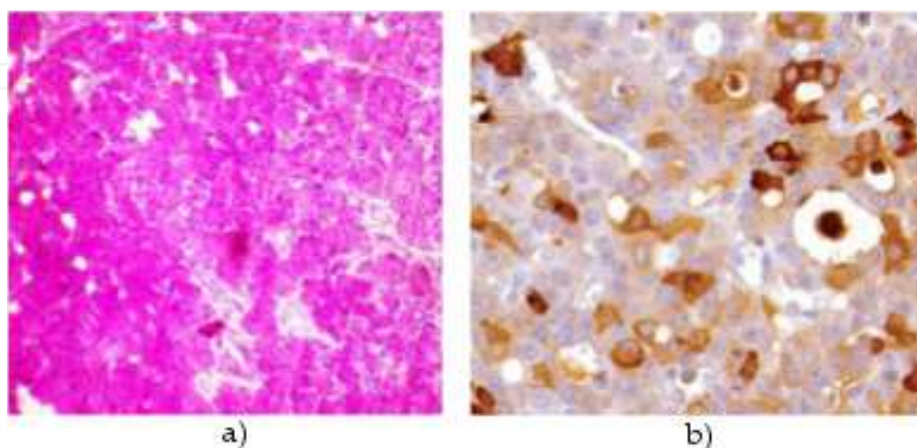


Figure 14. a) Serous acinar cells have abundant pale to basophilic, heavily granular cytoplasm (H&E). b) Trypsin is detectable in acinar cells.

4. Soft tissue tumors

The most common soft tissue tumors needing IHC are:

- Lobular capillary hemangioma
- Fibrosarcoma
- Angiosarcoma
- Kaposi Sarcoma
- Leiomyosarcoma
- Synovial Sarcoma
- Rhabdomyosarcoma
- Granular Cell Tumor

4.1. Lobular capillary hemangioma

4.1.1. Definition

Lobular capillary hemangioma previously commonly referred to as “pyogenic granuloma,” is a reactive soft tissue growth with a predilection for the oral cavity that is histologically characterized by a lobular arrangement (Figure15).

4.1.2. Immunohistochemical stains

Positive for endothelial markers including factor VIII-related antigen and CD31 of proliferating small blood vessels. [17-19]

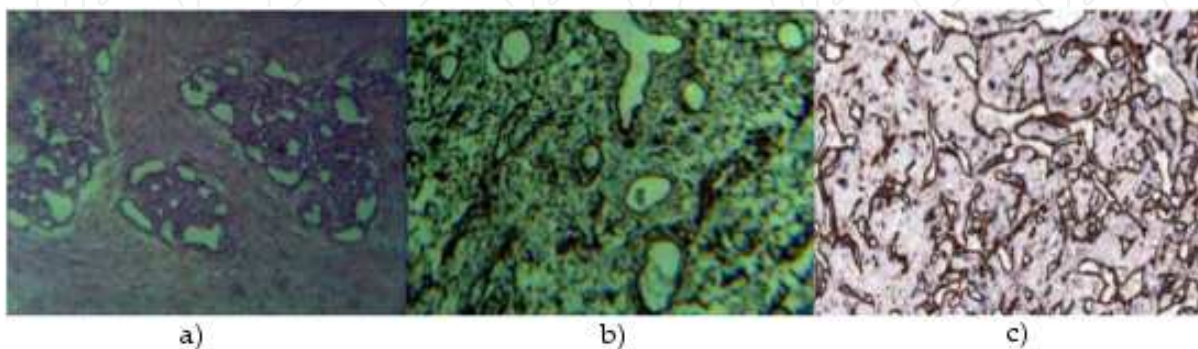


Figure 15. a) H&E capillary hemangioma b) CD31 highlights the endothelial cell C) Factor VIII noted in the endothelial cells.

4.2. Fibrosarcoma

4.2.1. Definition

Malignant neoplasm with only fibroblastic/myofibroblastic differentiation (Figure 16).

4.2.2. Immunohistochemical stains

Vimentin, and rarely, focal actin positivity. [40, 41]

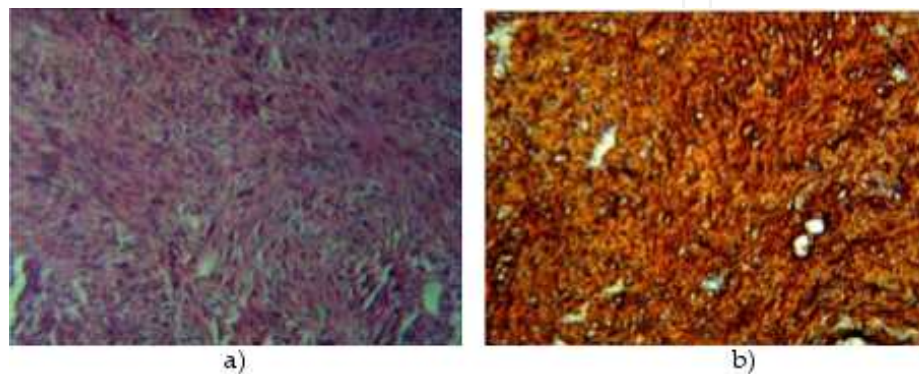


Figure 16. a) Hypercellular tumor, showing spindle cells. b) Vimentin is highly positive

4.3. Angiosarcoma

4.3.1. Definition

Uncommon, high-grade malignant vascular neoplasm, occasionally associated with radiation.

4.3.2. Immunohistochemical stains

Positive with CD34, CD31, factor VIII-RAg, vimentin, podoplanin. ERG shows nuclear positivity in nearly 100% of angiosarcomas. FLI1 expression is found in as many as 100% of angiosarcomas, but utility is limited by poor specificity for vascular lesions. CD31 expression is found in more than 90% of angiosarcomas (Figure 17).

VEGFR3 expression is found in approximately 50% of angiosarcomas, [42-50]

4.4. Kaposi sarcoma

4.4.1. Definition

Kaposi sarcoma is a malignant neoplasm of endothelial cells. Oral lesions are commonly multifocal. Early lesions: are flat, red, and asymptomatic. Older lesions: larger, darker, nodular, and ulcerated. KS is common in patients with AIDS.

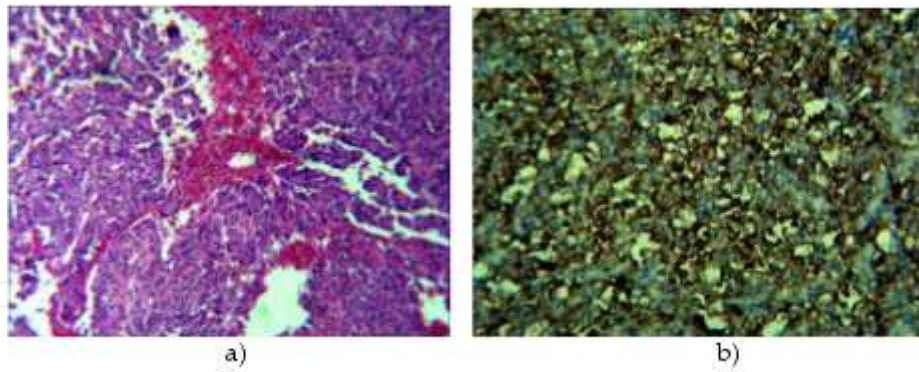


Figure 17. a) Richly vascularized tumor with open vascular channels and mitotic figures b) CD 31 is positive.

4.4.2. Immunohistochemical stains

Human herpes virus 8 has variable expression for endothelial markers (CD31, CD34)[17, 18, 19, 48, 51] (Figure 18).

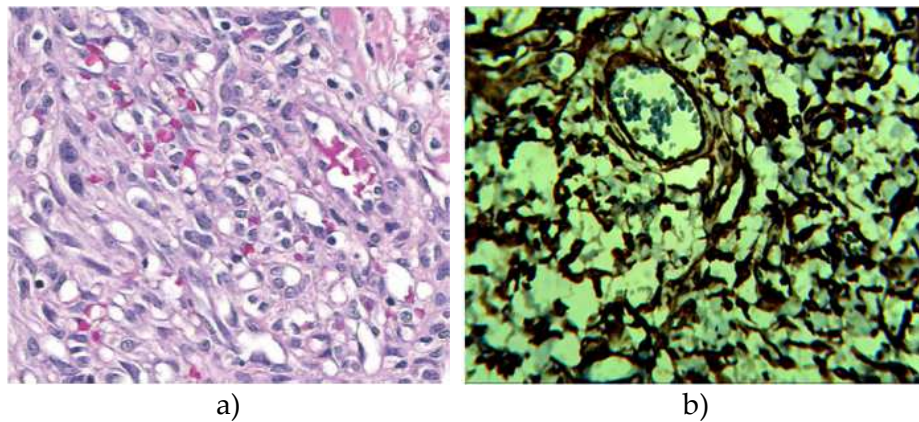


Figure 18. a) Nodular aggregates of spindle cells forming slit-like spaces (H&E). b) CD34 is positive.

4.5. Leiomyosarcoma

4.5.1. Definition

Malignant tumor of smooth muscle

4.5.2. Immunohistochemical stains

Currently, IHC confirmation of smooth muscle differentiation in LMS is based on the demonstration of desmin, α -SMA, muscle actin (HHF-35), and h-Caldesmon PAS with diastase will highlight intracellular glycogen. Tumor cells will be strongly and diffusely reactive with vimentin and actins (smooth muscle, muscle-specific), while variably positive for desmin [49, 50, 51, 52, 53, 54] (Figure 19) [52-57].

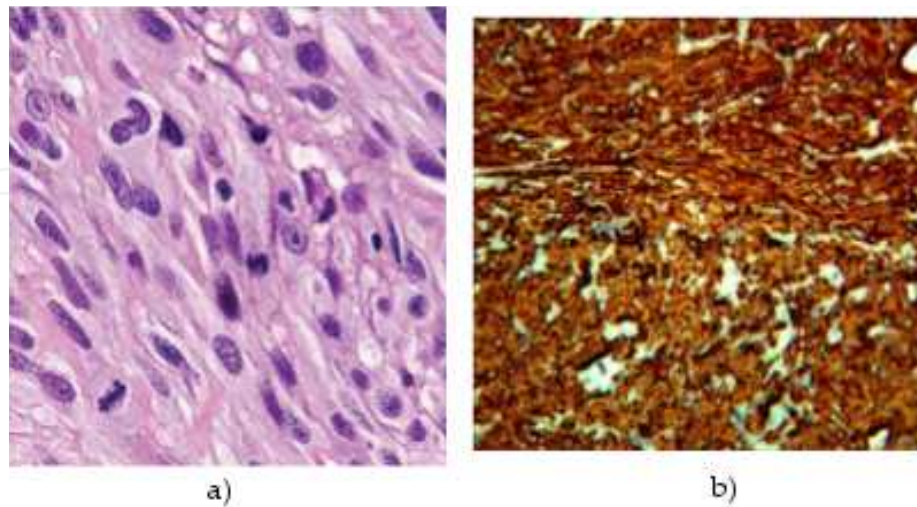


Figure 19. a) Spindle cell population. b) Desmin reactivity.

4.6. Synovial sarcoma

4.6.1. Definition

Synovial sarcoma is a malignant soft tissue tumor that shows epithelial and mesenchymal differentiation and has distinct clinical, genetic, and morphologic features.

Although it was once thought that synovial sarcoma arose in association with synovium, it is now well known that this is not the case and that these tumors may arise at any anatomic location.

4.6.2. Immunohistochemical stains

Morphologically, synovial sarcoma takes three main forms: 1) biphasic, 2) monophasic, and 3) poorly differentiated. Biphasic synovial sarcoma (BSS) consists of a fascicular spindle cell component and an epithelial component that usually shows glandular differentiation, whereas monophasic synovial sarcoma (MSS) lacks the epithelial component. The glandular component of synovial sarcoma expresses cytokeratins, including AE1/AE3. EMA expression is typically observed in both BSS and MSS. However, unlike its biphasic counterpart, MSS tends to be focally and inconsistently reactive for cytokeratins.

In particular, MSS may show reactivity for simple keratins: CK7, CK8, CK18, and CK19. S-100 protein expression is found in approximately 30% of synovial sarcomas. CD99 is commonly observed in MSS, but expression of this marker is also shared by some other spindle cell neoplasms. Strong positivity for BCL2 protein has also been noted in the spindle cell component of synovial sarcoma. [55-58]. TLE1 is positive in synovial sarcoma (Figure 20).

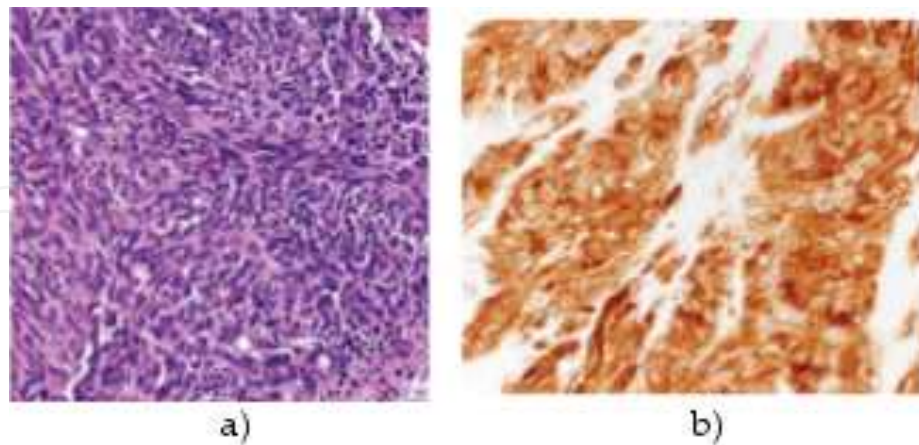


Figure 20. a) Spindle or epithelioid cells show a predominantly nested growth pattern. b) TLE1 is positive

4.7. Rhabdomyosarcoma

4.7.1. Definition

A malignant neoplasm with skeletal muscle phenotype: Embryonal type (80%): Alveolar type (20%)

4.7.2. Immunohistochemical stain

MYOD1, SMA positive A variety of myoid markers are positive (desmin, myogenin, MyoD1, myoglobin, actins), but it is important to remember that AE1/AE3, CAM5. 2, and CD56, along with synaptophysin, may be focally positive in some cases. [59, 60, 61] (Figure 21)

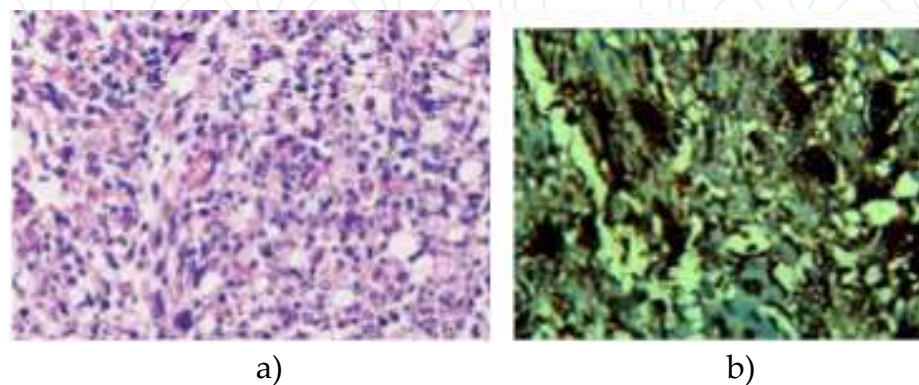


Figure 21. a) Mesenchymal cells and rhabdomyoblasts b) Desmin

4.8. Granular cell tumor

4.8.1. Definition

This is an uncommon tumor composed of poorly demarcated granular cells, thought to be Schwann-cell derived, that frequently arise below a mucosa, the latter often showing pseudoepitheliomatous hyperplasia. Granular cell tumor tends to affect the oral cavity (tongue most commonly). Tumors are usually smooth surfaced, poorly demarcated, and are often polypoid, and measure from 1 to 2 cm.

4.8.2. Immunohistochemical stains

The neoplastic cells yield a strong and diffuse nuclear and cytoplasmic S-100 protein reaction and are also positive for CD68, NSE, α -1-antitrypsin [17-19, 62] (Figure 22).

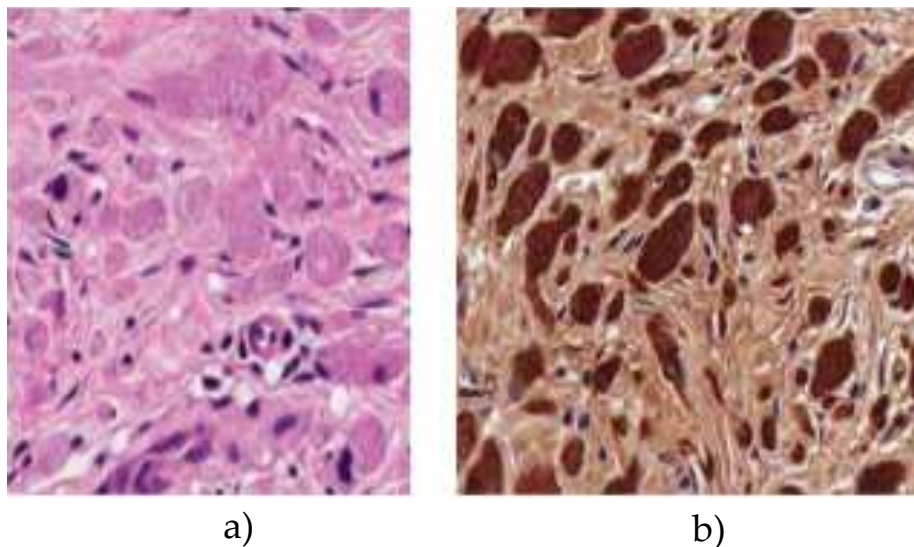


Figure 22. a) Polygonal granular cells H&E b) neoplastic cells with s-100

5. Hematologic disorders

The common hematologic disorders that need IHC stains are;

- Hodgkin's lymphoma
- Non – Hodgkin's lymphoma
- Extranodal NK/T-Cell lymphoma, (angiocentric T-cell lymphoma) Midline lethal granuloma
- Burkitt's lymphoma

5.1. Hodgkins lymphoma

This almost always begins in the lymph nodes, and any lymph node group is susceptible.

The most common sites of initial presentation are the cervical and supraclavicular nodes (70% to 75%). Hodgkin's lymphoma is currently classified in the following manner:

- **Lymphocyte-rich**
- **Nodular sclerosis**
- **Mixed cellularity**
- **Lymphocyte depletion**

5.1.1. Immunohistochemical stains

The antibodies most commonly used for diagnosing HL are Ber-H2 (CD30), LeuM1 (CD15), LCA (CD45), L26 (CD20), CD75 (LN1), CD74 (LN2), PAX5, CD3, UCHL1 (CD45RO), ALK, fascin, and EBV-LMP1. EMA and CD57 can be used to recognize NLPHL.

Monoclonal antibody LN1 reacts with H/RSCs in approximately one third of HL cases, most frequently in cases of NLPHL (>75% of cases)(Figure 23). [17-19]

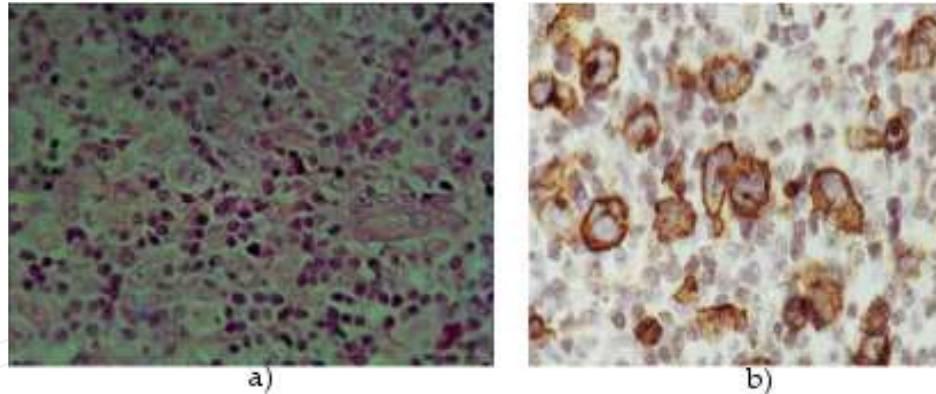


Figure 23. a) Hodgkin/Reed-Sternberg cells b) antigenic Reed-Sternberg cells for CD15

5.2. Non- Hodgkins lymphoma

5.2.1. Definition

Non-Hodgkin's lymphoma most commonly develops in the lymph nodes, In the oral cavity. Lymphoma usually appears as extranodal disease. The malignancy may develop in the oral soft tissues or centrally within the jaws; they most commonly affect the buccal vestibule, posterior hard palate, or gingiva.

5.2.2. Immunohistochemical stains

Small Cell Lymphoid Neoplasms

The lymphoma cells express pan-B-cell antigens (CD19, CD20, CD22, PAX-5). Mantle cell lymphoma (MCL) expresses pan-B-cell antigens (CD19, CD20, CD22), CD5, CD43, Bcl-2, and cyclin D1.

Nodal marginal zone lymphoma (NMZL) will typically express pan-B-cell antigens that include CD19, CD20, PAX5, and CD79a;

Co-expression with Bcl-2 and CD43 is common and occurs in 50%. The vast majority of low-grade follicular lymphoma (FL) are positive for Bcl-2 small lymphocytic lymphoma (CLL/SLL) includes expression of CD5, CD23, CD19, CD43, and Bcl-2 and has a proliferation rate of less than 10%. [17-19] (Figure 24).

Large B-Cell Lymphoid Neoplasms

CD15 expression +

CD30 +

CD45 expression +

PAX5 strong, uniform + CD20 strong, uniform +.

CD79a expression +.

p63 +

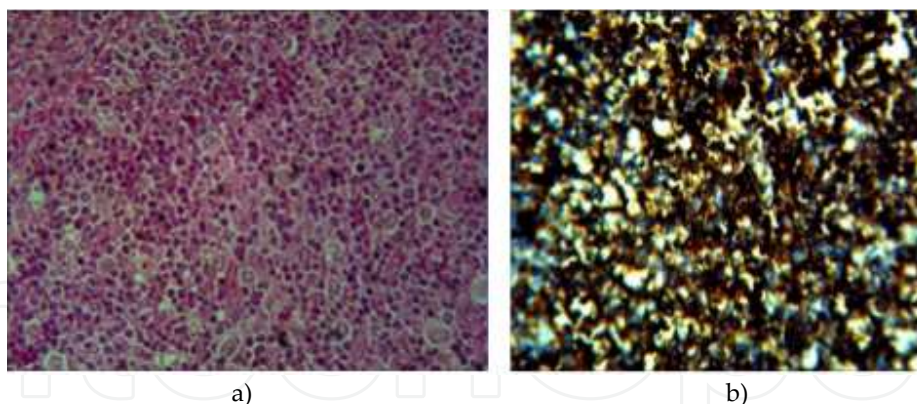


Figure 24. a) B-cell lymphoma (H&E) b) CD 20 is positive

T-Cell Lymphoid Neoplasms

Almost all peripheral T-cell lymphomas express pan-T-cell antigens CD3, CD2, and CD43. Anaplastic large-cell lymphoma (ALCL) is positive for CD30, and the expression should be strong and in at least 75% of the cells.

The neoplastic cells of angioimmunoblastic T-cell lymphoma (AITL) are positive for pan-T-cell antigens CD3, CD2, CD5, [17-19]

5.3. Extranodal NK/T-cell lymphoma, (angiocentric T-cell lymphoma) midline lethal granuloma

5.3.1. Definition

NK/T-cell lymphoma is the most common malignant nonepithelial neoplasm found in the upper respiratory tract and most commonly involves the nasal cavity, the maxillary sinus, nasopharynx, and salivary gland. This discussion will be limited to extranodal NK/T-cell lymphoma, nasal type (NK/T LNT), which is more common in the sinonasal region.

5.3.2. Immunohistochemical stains

NK cells express CD2, CD7, CD8, CD56, and CD57. They are positive for cytoplasmic CD3, but not surface CD3, and do not typically express CD5. The neoplastic counterpart, extranodal NK/T-cell lymphomas, express CD2, cytoplasmic CD3, CD56, and, in most cases, EBV. [17-19] (Figure 25, 26).

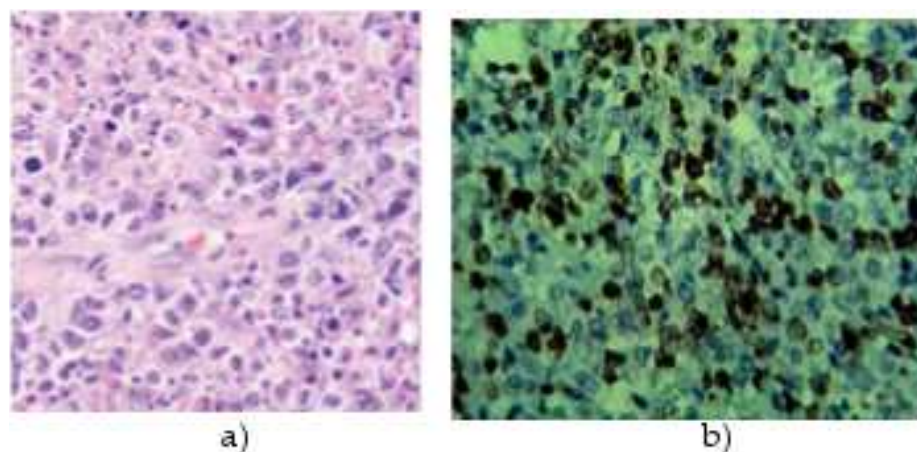


Figure 25. a) Extranodal natural killer/T-cell lymphoma b) CD3 staining is positive

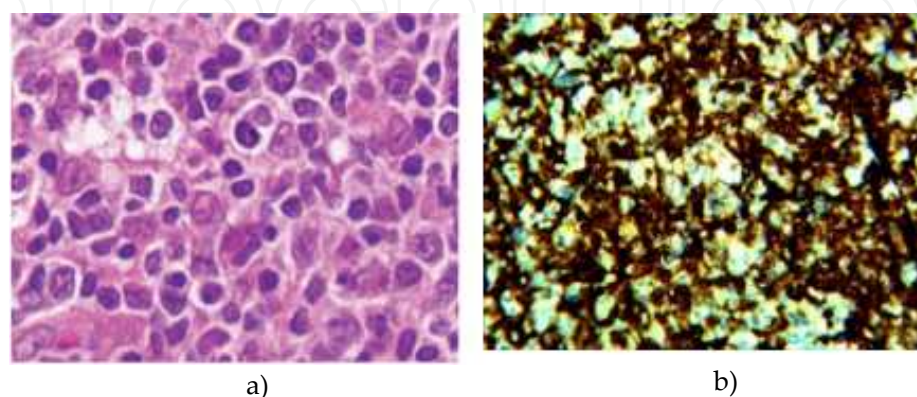


Figure 26. a) Atypical lymphoid cells(NK/T-CELL LYMPHOMA) b) Diffusely immunoreactive with CD3C

5.4. Burkitt's lymphoma

5.4.1. Definition

Burkitt's lymphoma is a malignancy of B-lymphocyte origin that represents an undifferentiated lymphoma. The tendency for jaw involvement seems to be age related: nearly 90% of 3-year-old patients have jaw lesions.

5.4.2. Immunohistochemical stains

There were statistically significant differences in the expression of CD10 (28/28 vs. 1/16), bcl-2 (3/28 vs. 11/16), MUM1 (5/28 vs. 15/16), a PI of 95.0% or more (27/28 vs. 2/16), and combined CD10+/bcl-2-/bcl-6+ (24/28 vs. 1/16) between BLs and DLBCL-HPSSs. Of the BLs, 7 (25%) of 28 and 26 (96%) of 27 were positive for EBER and c-myc rearrangement as compared with 0 of 16 and 1 (7%) of 15 DLBCL-HPSSs, respectively as compared with 0 of 16 and 1 (7%) of 15 DLBCL-HPSSs, respectively. [17-19, 63]

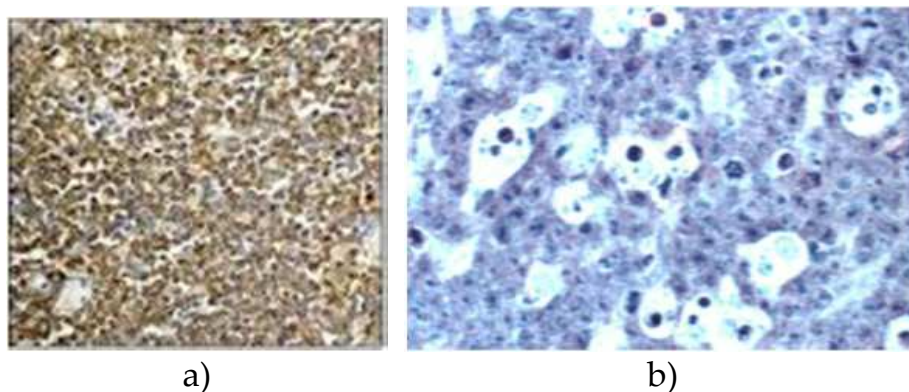


Figure 27. a) Burkitt's lymphoma. "starry-sky" appearance b) CD10 staining

6. Bone tumors

The common bone tumors needing IHC are:

- Osteosarcoma
- Chondrosarcoma
- Ewing sarcoma

6.1. Osteosarcoma

6.1.1. Definition

Osteosarcoma is the most common nonhematopoietic primary malignant bone tumor ; it is a malignant mesenchymal tumor producing osteoid from the tumor cells (Figure 28).

6.1.2. Immunohistochemical stains

CD99 positive; rare cytokeratin and smooth muscle actin reaction. Overall, the reported specificity of immunoreactivity for osteonectin and osteocalcin is approximately 40% and 95%, respectively, for the diagnosis of a bone forming tumor. A recent promising marker for identification of osteoblastic differentiation is SATB2, a nuclear matrix protein that plays a role in osteoblast lineage commitment. α -SMA and desmin, which can lead to misdiagnosis. [63-69]

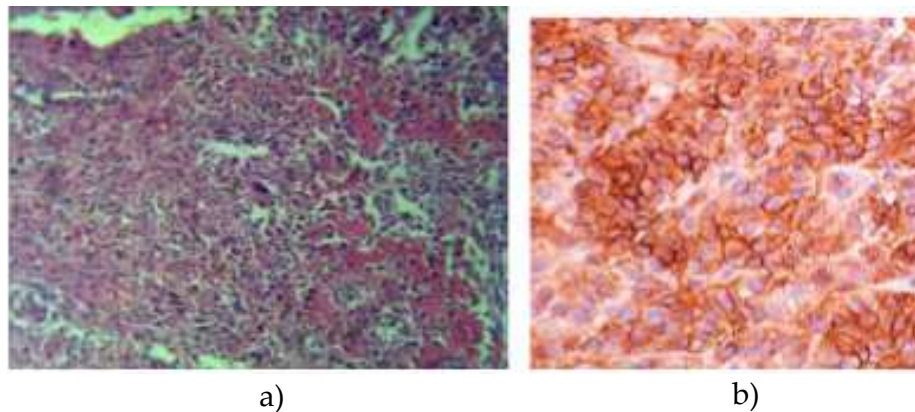


Figure 28. a) Osteosarcoma demonstrates irregular trabeculae of tumor osteoid arising from sarcomatous stroma. b) CD99 is positive

6.2. Chondrosarcoma

6.2.1. Definition

Chondrosarcoma is a malignant tumor of bone that shows pure cartilaginous differentiation. Secondary changes that include myxoid features, ossification, and calcification may be present. (Figure 29).

6.2.2. Immunohistochemical stains

Cartilage stains S100 protein positive Mesenchymal chondrosarcoma: Sox9, CD99, and Leu7 positive Although the cartilaginous component of mesenchymal chondrosarcoma is S-100 protein positive, the small-cell component expresses CD99, CD57, and NSE therefore immunohistochemically, there may also be overlap with Ewing sarcoma. However, unlike Ewing sarcoma, MCS is nonreactive for synaptophysin and also typically does not express desmin, actin, cytokeratin, or EMA. In addition, MCS lacks *EWSR1* gene rearrangements. However, a

recent study has identified a novel *HEY1-NCOA2* fusion in MCS which appears to be a consistent finding. [70, 71]

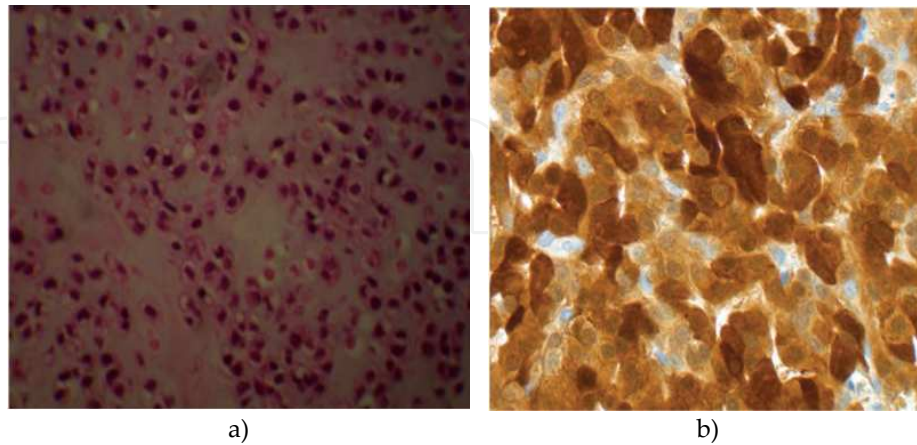


Figure 29. a) High-grade chondrosarcoma b) with marked S100 PROTEIN increase in cellularity and myxoid matrix

6.3. Ewing sarcoma

6.3.1. Definition

High-grade, primitive neuroectodermal neoplasm (Figure 30)

6.3.2. Immunohistochemical stains

Positive: FLI1 (nuclear), CD99, vimentin; rarely keratin. May react with other neural markers (NSE, synaptophysin, S100 protein, NFP, GFAP, chromogranin). [72-79]

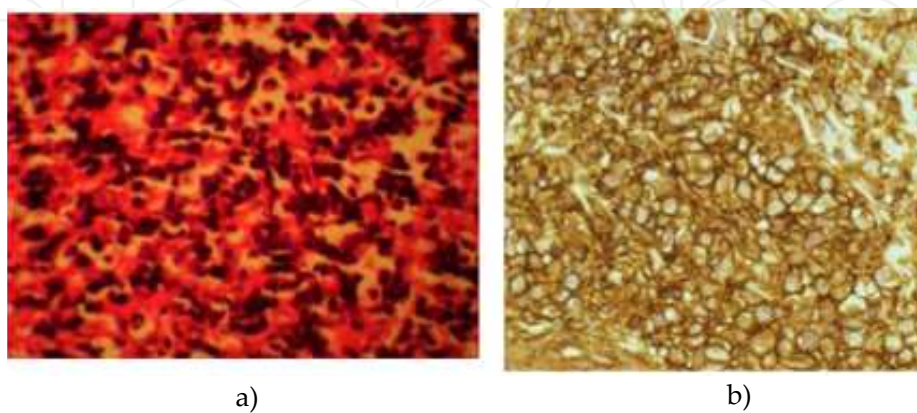


Figure 30. a) Small nucleoli scant cytoplasm with mitosis b) diffuse strong membranous expression of CD99

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