

Pathology of the Larynx

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I. Non-Neoplastic Lesions

A. Vocal Cord Polyps and Nodules

1. Nodules and polyps have essentially the same histologic appearance, but the clinical settings are different.
2. A nodule is a bilateral thickening of the opposing surfaces of the Vocal fold mucosa, usually in the middle third. The lesions may be edematous, gelatinous, or hemorrhagic. Usually the size is no more than a few millimeters.
3. Vocal cord polyps are generally unilateral (>90%) and are most often seen in Reinke's space or the ventricular space. They are usually seen on the anterior half of the cord and may be sessile or pedunculated. Epithelium is usually unremarkable; the underlying stroma is edematous, with myxoid matrix. Eventually vascular proliferation and fibrosis or hyaline change develop. The predominant patterns seen are on a spectrum: edematous, vascular, hyaline, fibrous.

B. Contact Ulcer

1. A benign ulcerative lesion which produces a nodule.
2. Etiology: Entubation, voice abuse, gastroesophageal reflux.
3. M>F, generally adults. Most common site is along *posterior* aspect of one or both true vocal cords.
4. Symptoms: hoarseness, dysphagia, dysphonia, obstruction, choking.
5. Gross: Ulcerated polypoid mass up to 3 cm in diameter.
6. Micro: Ulcerated mucosa with underlying florid granulation tissue with radiating vascular pattern. Stromal cells may be plump and endothelial cells may be large as well.
7. DDX: Spindle cell carcinoma (sarcomatoid carcinoma) of the larynx.
8. Treat the underlying cause.

C. Amyloidosis

1. Accumulation of extracellular proteinaceous material as an isolated primary disease process or secondary to systemic disease or malignancy.
2. M>F; 5th-6th decades. Presents with hoarseness.
3. False vocal cord most common site, but may present with a diffuse infiltration of the subglottic region. The deposits are often multifocal, with a pale waxy cut surface.

4. Micro: Extracellular accumulation of acellular eosinophilic material, often perivascular or periglandular in distribution, with associated lymphocytes and plasma cells. Foreign body giant cell reaction may be present. Congo red stain positive with apple green birefringence.
5. Differential dx: Important to consider possibility of underlying malignant plasma cell neoplasm/lymphoma.
6. 15% of patients with laryngeal amyloidosis have other sites involved.

II. Neoplasms

A. Rhabdomyoma, Adult type

1. Benign tumor of skeletal muscle.
2. Less common than rhabdomyosarcomas. M>F; over age 40. Seen especially in neck, pharynx, larynx, tongue, FOM, soft palate.
3. Gross: Well-circumscribed, but not encapsulated brown tumor, resembling muscle.
4. Micro: Large polygonal cells with fibrillar eosinophilic cytoplasm, often with cross-striations. One or two nuclei usually at periphery of cell.
5. Immunostains: Desmin, actin, myoglobin, and other muscle markers +.
6. DDX: Granular cell tumor, alveolar soft part sarcoma.
7. Treatment : Cured by complete surgical excision.

B. Laryngeal Papillomatosis

1. Most common benign neoplasm of the larynx.
2. Associated with HPV: Type 6/11 most common. More aggressive disease possibly associated with Type 16 and 18.
3. May involve any portion of upper and lower respiratory tract, but usually begins in glottis. Extension into bronchial tree and lung may be fatal, even in benign disease.
4. Cases usually present in infancy or early childhood; however, identical lesions may appear at any age; adult forms do not tend to spread and recur as extensively as childhood forms.
5. Gross: Warty polypoid lesions from tiny to 1 or more cm in diameter.
6. Micro: Rounded papillary proliferations of nonkeratinizing squamous epithelium. Minor areas of keratinization may be seen. Clear koilocytotic change is uncommon, but minor cytologic atypia is common. Marked cytologic atypia, especially in children, does not necessarily imply malignant or premalignant change. In adults it is more worrisome.

7. Treatment: Endoscopic removal of gross lesions with laser, may need to be done every few months. Recent intralesional injection with anti-virals has shown great promise.
8. Prognosis: 2% incidence of carcinoma. 2-14% mortality; 2-15% extend into tracheobronchial tree. May regress at puberty or later.

C. Granular Cell Tumor

1. Benign (usually) tumor of Schwann cell origin. In the H&N, skin is most common; tongue is more common than larynx.
2. F>M. Most in young adults. Usually presents as a painless mass.
3. Micro: Pseudoepitheliomatous hyperplasia often present, may mimic SCCa. Tumor cells have eosinophilic granular cytoplasm and round centrally placed nucleoli. Not encapsulated, may appear infiltrative and involve nerves. Malignancy is rare; they are more cellular, with nuclear pleomorphism, necrosis, mitotic activity, and have prominent nucleoli (DDx is paraganglioma and alveolar soft part sarcoma).
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7. Special Stains: PAS+diastase resistant granules=lysosomes. S100 positive.
8. Treatment: Surgical excision for benign lesions.

D. Squamous Cell Carcinoma

1. >95% of all laryngeal carcinomas.
2. M>F; 5th-7th decades.
3. Strongly linked to tobacco and/or alcohol use.
4. Location: Glottic-60-65%, Supraglottic-30-35%, Subglottic-5%.
5. SX: Hoarseness, dysphagia, dyspnea, hemoptysis.
6. Gross: Exophytic, fungating, endophytic, or ulcerated
7. Micro: Keratinizing, non-keratinizing squamous proliferation associated with infiltrative growth or exophytic growth. Some poorly differentiated examples have little evidence of squamous differentiation.

8. Diff Dx: Pseudoepitheliomatous hyperplasia.
9. Treatment stage dependent.
10. Prognostic factors: Site, size, grade, margins, metastasis, multiplicity of primary lesions.
11. Aggressive variants: Basaloid squamous cell carcinoma and adenosquamous carcinoma.
12. Transglottic examples more aggressive- only 40% 5-year survival.

E. Spindle Cell Squamous Carcinoma (Sarcomatoid Carcinoma)

1. Squamous cell carcinoma with a sarcomatoid pattern. May occur in other mucosal sites of upper respiratory tract; larynx most common.
2. 85% in males. 6th to 8th decades. No specific correlation of this pattern with risk factors; some in area of prior irradiation.
3. Usually exophytic or polypoid 1-6 cm in diameter. Often do not invade deeply or extend into extralaryngeal soft tissue.
4. Tends to arise from anterior aspect of vocal cord unlike contact ulcer.
5. Micro: Spindle cells or pleomorphic cells with high cellularity and high mitotic rate, may have areas of osseous or cartilagingous differentiation. Look for areas of squamous cell carcinoma or overlying dysplasia.
6. Immunostains: May or may not be cytokeratin positive. Don't let this dissuade you. Primary sarcomas (except well-differentiated chondrosarcomas of the laryngeal skeleton) are really rare.
7. Treatment: Surgical excision; radiation may be added based on stage.
8. Prognosis is generally poor, but the polypoid vocal cord lesions may do better.

F. Verrucous Carcinoma

1. A very well-differentiated squamous cell carcinoma with a favorable prognosis.
2. This is a rare tumor, so beware of making dx.
3. M > F. 6th-7th decades. May be related to tobacco use and viral agents (not proven).
4. Most common sites are glottic larynx and buccal mucosa and gingival.
5. Gross: Warty appearing with lots of surface keratinization. Usually broad-based.
6. Micro: Strict requirements: Uniform cells without dysplasia or mitoses; marked surface keratinization in church spire pattern; broad or bulbous rete pegs with a pushing rather than infiltrating border. In addition, usually chronic inflammation at base.

7. The presence of dysplastic nuclei or infiltrative pattern means diagnosis is an ordinary squamous cell carcinoma.
8. Treatment: Surgical excision. Radiation can be used for advanced disease in poor surgical candidates. Metastases to regional nodes are rare, but may occasionally occur. Distant mets do not occur in verrucous carcinoma.
9. Prognosis: Excellent if completely excised. Rare cases undergo anaplastic transformation, and will then behave as a typical squamous carcinoma.

G. Neuroendocrine Carcinoma

1. Tumors with both epithelial and neuroendocrine differentiation. May be seen anywhere in upper respiratory tract mucosa.
2. Three categories, based on degree of differentiation: Carcinoid (Well-differentiated); Atypical carcinoid (Moderately-differentiated), and Small cell carcinoma (Poorly-differentiated).
3. Association with smoking.
4. M>F; 6th decade and older.
5. Micro: Neuroendocrine features ranging from carcinoid-like to small cell undifferentiated carcinoma.
6. Immunohistochemistry helpful: Chromogranin, cytokeratin positive; calcitonin positive (no serum elevation).
7. Prognosis: Carcinoid-excellent; atypical carcinoid-62% 4-yr survival; small cell-16% 2-yr survival.
8. Treatment: Surgery for carcinoid and atypical carcinoid. Radiation and chemotherapy for small cell ca.