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Tissue Talk: Uncovering Tissue Secrets Through Biopsy- A Review

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ABSTRACT:

Accurate diagnosis of oral lesions requires a well-executed surgical biopsy and histopathological examination. However, inadequate biopsy techniques, poor tissue handling, and insufficient patient information can lead to misdiagnosis. This article reviews clinical surgical biopsy procedures and discusses three tissue stabilization methods, highlighting the importance of clinician experience and preference in selecting the appropriate tool for successful outcomes.

KEYWORDS: Oral cancer, biopsy, biospecimens

INTRODUCTION:

Oral cancer is a malignant tumor that occurs on the lip or in the mouth. Globally, oral and pharyngeal cancers are the sixth most common type of cancer. However, their prevalence varies by region, ranking as high as first and as low as eleventh, with Southcentral Asia and Melanesia having the highest incidence rates[1].

Between 1990 and 2017, the incidence, mortality, and disability-adjusted life years (DALYs) of oral cancer doubled. According to recent statistics, the age-standardized incidence rate of oral cancer is approximately 2.4 per 100,000 people, while the age-standardized disability-adjusted life years are around 64.0 per 100,000 person-years[1].

Oral cancer is most prevalent in Asia, with high mortality rates. Approximately 80-90% of oral cancers are oral squamous cell carcinoma (OSCC), accounting for 3% of global cancers[1].

The World Health Organization defines precancerous conditions as Oral Potentially Malignant Disorders (OPMDs), which may exhibit epithelial dysplasia[2]. OPMDs can occur in various tissues, including the tongue, lips, buccal mucosa, gingiva, and palate.

Common OPMDs include:

- Leukoplakia
- Erythroplakia
- Proliferative verrucous leukoplakia
- Oral lichen planus
- Oral submucous fibrosis

Leukoplakia is the most common OPMD, with a global prevalence of 1.7-2.7% and a malignant conversion rate of 1.36%. Early detection is crucial, as it significantly improves treatment outcomes[3]. Research shows that:

- 7.9% of OPMD cases progress to carcinoma with moderate or severe dysplasia
- 3-year survival rate for early-stage cancer is 92.2%
- 3-year survival rate for late-stage cancer is 70.3%

However, early-stage cancers are often asymptomatic, making diagnosis challenging.

PRINCIPLES OF ORAL BIOPSY:

When evaluating patients, dentists or oral surgeons should thoroughly review their medical and dental history, paying close attention to systemic diseases such as:

- Seizures
- Asthma
- Cardiovascular diseases (e.g., myocardial infarction, angina pectoris)
- Stroke
- Rheumatoid fever
- HIV disease
- Tuberculosis
- Hepatitis

Additionally, they should inquire about the patient's oral habits, including:

- Betel quid chewing
- Tobacco smoking
- Alcohol consumption

To diagnose oral lesions, clinicians should thoroughly assess their size, depth, location, color, consistency, surface texture, mobility, and other clinical characteristics[4].Before performing a biopsy, patients must provide informed consent, understanding the potential complications, including pain, bleeding, swelling, infection, scarring, and aesthetic concerns[4].

Excisional biopsy should be avoided if oral malignancy is suspected to preserve the lesion's borders for future surgery[5].

Incisional biopsy is often used for lesions with possible malignancy or large lesions, but may lead to underdiagnosis[5].

To ensure accurate diagnosis, it's essential to obtain sufficient tissue samples for histopathological examination. However, accessing certain oral lesion locations, such as the floor of the mouth, lip, gingiva, or mental area, can be challenging due to limited accessibility, bleeding control, and potential damage to surrounding structures like the submandibular duct or mental nerve[6].

PROCEDURES:

The oral biopsy procedure involves several key steps:

1. Selecting the biopsy site
2. Preparing the operation field
3. Administering anesthesia
4. Stabilizing the tissue
5. Incising or excising the lesion
6. Handling the biopsy tissue
7. Achieving hemostasis
8. Closing the surgical wound

Tissue stabilization is a critical aspect of the procedure, as it ensures clear visibility and accessibility of the surgical field, keeping the targeted tissue in place and preventing movement during the biopsy[6].

TISSUE BIOPSY:

Tissue biopsy, particularly surgical biopsy, remains the most reliable method for oral cancer diagnosis, involving the removal of soft tissues or lymph nodes through surgery or specialized instruments[7]. Various biopsy methods exist, including punch, lymph node, brush, and needle aspiration biopsies. The obtained tissue is typically analyzed using frozen sections (FS) with H&E staining, considered the gold standard for intraoperative tumor evaluation, although this method can be time-consuming and expensive, prompting exploration of alternative methods like multi-staining (MS)[7].

Researchers have utilized various techniques for cancer screening and diagnosis, including Visual Inspection with Acetic Acid (VIA) and Visual Inspection with Lugol's Iodine (VILI), which have shown high diagnostic accuracy in cervical cancer screening and distinguishing epithelial carcinoma and dysplasia from benign mucosal lesions[8]. Furthermore, advanced techniques like qPCR and immunofluorescence staining have been employed to analyze genetic alterations and mitochondrial DNA amounts in normal and cancerous tissues.

- Surgical biopsy
- Punch biopsy
- Needle aspiration biopsy
- Sentinel lymph node biopsy
- Brush biopsy

SURGICAL BIOPSY:

A surgical biopsy is a medical procedure that involves removing a sample of tissue from the body through surgery. The purpose of a surgical biopsy is to examine the tissue for abnormal cell growth, cancer, or other diseases.

Types of Surgical Biopsy
1. Incisional Biopsy: A sample of tissue is removed from the affected area for examination.
2. Excisional Biopsy: The entire affected area is removed for examination.
3. Needle Biopsy: A needle is used to remove a sample of tissue.
4. Aspiration Biopsy: A needle is used to remove a sample of fluid or tissue[9].

Indications:
1. Cancer Diagnosis: To diagnose cancer or precancerous lesions.
2. Disease Diagnosis: To diagnose conditions such as inflammatory diseases or infections.
3. Abnormal Growth: To examine abnormal growths or tumors[9].

Procedure:
1. Preparation: The patient is given general anesthesia or local anesthesia to numb the area.
2. Surgical Incision: A surgical incision is made to access the affected area.
3. Tissue Removal: The biopsy sample is removed using one of the above-mentioned methods.
4. Stitching: The wound is closed with stitches.
5. Recovery: The patient is monitored for bleeding and discomfort[9].

Risks and Complications:
1. Bleeding: Mild bleeding is common, but heavy bleeding is rare.
2. Infection: As with any surgical procedure, there is a risk of infection.
3. Scarring: The biopsy site may scar.
4. Nerve Damage: There is a small risk of nerve damage, which can cause numbness or tingling[9].

PUNCH BIOPSY:

Usually a variation of an incisional biopsy, which removes a piece of the lesion using specialized punch-type forceps, it can be either incisional or excisional.6
With this technique, tiny tissue segments from big lesions where excision is not advised or from inaccessible lesions are filed out by the surgical instrument. Because this tool frequently causes deformation of the lesion, this technique is rarely applied in the oral cavity.

PRINCIPLE:

Using this technique, the punch is held perpendicular to the skin and twisted slowly while applying intense downward pressure. The punch is forced downward until it reaches the subcutaneous fat. The pedicle is severed and the tissue column that was cut in the punch is raised. The tissue is then cautiously taken out of the punch[10].

NEEDLE ASPIRATION BIOPSY:

Advantages:
Patients handle it well, and many of them have had major head and neck operations before.
It is a straightforward outpatient treatment with a low risk of infection and quick recovery. With this method, the surgeon might be able to get tissue for a surgical biopsy-only histological diagnosis. It has an advantage over FNAC in that most practicing pathologists with little knowledge of cytopathology may more easily understand the data[10].

Disadvantages:
Reports that are falsely unfavorable. The potential for tumor spread[10].

SENTINEL LYMPH NODE BIOPSY:

A Sentinel Lymph Node Biopsy (SLNB) is a medical procedure that involves removing the first lymph node (or nodes) to which cancer cells are likely to spread from a primary tumor. The purpose of SLNB is to determine if cancer has spread to the lymph nodes[10].

Procedure:
1. Preparation: The patient is given local anesthesia and/or sedation to numb the area and relax.
2. Injection of Radiotracer: A small amount of radioactive material (radiotracer) is injected near the tumor site.
3. Lymph Node Identification: The radiotracer travels to the sentinel lymph node, which is then identified using a special camera or probe.
4. Removal of Sentinel Lymph Node: The sentinel lymph node is removed and sent to a laboratory for examination[10].

Indications:
1. Breast Cancer: SLNB is commonly used to diagnose and stage breast cancer.
2. Melanoma: SLNB is used to diagnose and stage melanoma, a type of skin cancer.
3. Other Cancers: SLNB may also be used to diagnose and stage other types of cancer, such as colon, lung, and thyroid cancer[10].

BRUSH BIOPSY:

A punch biopsy is a medical procedure that involves removing a small sample of tissue from the skin or mucous membranes using a specialized tool called a punch biopsy needle. The purpose of a punch biopsy is to examine the tissue for abnormal cell growth, cancer, or other diseases[8].

Procedure

1. Preparation: The patient is given local anesthesia to numb the area.
2. Cleaning and Preparation of the Site: The area is cleaned and prepared for the biopsy.
3. Punch Biopsy Needle Insertion: The punch biopsy needle is inserted into the skin or mucous membrane, and a small sample of tissue is removed.
4. Tissue Removal: The tissue sample is removed and sent to a laboratory for examination[8].

Indications

1. Skin Lesions: Punch biopsy is commonly used to diagnose skin lesions, such as moles, rashes, or growths.
2. Oral Lesions: Punch biopsy is used to diagnose oral lesions, such as ulcers, growths, or white patches.
3. Mucous Membrane Lesions: Punch biopsy is used to diagnose lesions on the mucous membranes, such as the lining of the mouth, nose, or vagina[8].

TECHNIQUES:

A wide range of diagnostic techniques are utilized in oral pathology, including histopathological staining (H&E, IHC, Lugol's iodine), molecular diagnostics (RT-PCR, PCR, FISH), immunological techniques (ICC, immunofluorescence), cytological methods (cytological smears, Trypan blue exclusion assay), and various imaging and diagnostic techniques (VIA, SSOCT, ultrasound, near-infrared imaging)[4].

ADVANTAGES:

- Suitable for localized lesion
- Most accurate for
- assessment
- A small fragment of tissue is
- sufficient

LIMITATIONS:

- Bleeding
- Risk of infection
- Time intensive
- Delayed diagnosis
- Require greater technical efforts

Liquid biopsy:

Liquid biopsies offer a non-invasive, painless, and low-risk method for early cancer detection by analyzing fluid samples such as saliva, blood, urine, or surgical drainage for cancer markers. Although liquid biopsies have the potential for early diagnosis, they require initial histologic diagnosis and can be prone to over-interpretation, low sensitivity, and high false results, necessitating advanced technical expertise[7]

Types of Liquid Biopsy

1. Circulating Tumor DNA (ctDNA) Analysis: ctDNA is DNA released by cancer cells into the bloodstream. Analyzing ctDNA can help identify genetic mutations and monitor cancer progression.

2. Circulating Tumor Cell (CTC) Analysis: CTCs are cancer cells that break away from the primary tumor and circulate in the bloodstream. Analyzing CTCs can provide information on cancer cell biology and behavior.

3. Exosome Analysis: Exosomes are small vesicles released by cells, including cancer cells. Analyzing exosomes can provide insights into cancer biology and identify potential biomarkers.

4. MicroRNA (miRNA) Analysis: miRNAs are small RNA molecules involved in gene regulation. Analyzing miRNAs in bodily fluids can help identify cancer biomarkers[8].

Type of Sampling

Blood, saliva, urine, and surgical drain fluid collection.

TECHNIQUES:

Avariety of laboratory tests and techniques are employed in oral pathology, including molecular assays (qPCR, RT-qPCR, ddPCR), protein analysis (Western blot, ELISA), microbial detection (bacterial colony count), and biochemical assessments (total protein estimation, biochemical analysis of saliva), as well as advanced technologies like flow cytometry, micro-Raman, and proteomic analysis[9].

ADVANTAGES:

- Non-invasive or less invasive
- No/less bleeding
- Easily collected
- Easily transported
- Detect various biomarkers
- Tracking dynamic changes

LIMITATIONS:

- Inaccurate
- Low sensitivity
- Need an initial pathological diagnosis

CONCLUSION:

While invasive biopsies remain the gold standard for oral cancer diagnosis, non-invasive methods like liquid biopsy and brush biopsy are gaining traction and are expected to become increasingly adopted in clinical practice. However, there is a need for standardization and harmonization of downstream molecular analyses to ensure accurate and reliable results from oral cancer biopsy samples[10].

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