Chairside diagnostic aids in oral precancerous and cancerous lesions.

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Abstract : Chair side investigations are simple; rapidly doing procedures and require inexpensive equipment's. They do not need specialized training. It is carried out conveniently in your dental office set up or clinic. For the dental profession, it is really challenging and highly important to diagnose oral conditions, precancer or oral cancer particularly in its early stage of the disease. Early screening and advanced diagnostic tool play an important role in the early diagnosis, treatment planning and for better prognosis of patients suffering from oral cancer. The present literature review provides the classification of Chairside investigations oforal cancer and some commonly used investigation in brief.

Keywords: Chairside investigations, staining, biopsy.

INTRODUCTION:

Oral medicine involves the diagnosis and treatment of complex diagnostic medical disorders affecting the mouth and jaws. In day-to-day clinical practice, dental and medical practitioners often encounter a wide spectrum of oral mucosal lesions. Mucosal disorders may occasionally be diagnosed correctly from a brief history and rapid clinical examination, but this approach is most often insufficient and leads to incorrect diagnosis and improper management. When a careful and detailed history is taken, it provides a more information and guides the clinician during the clinical examination.[1] Investigations of a patient with an oral lesion include chair side investigations, radiographic investigations and laboratory investigations.[2] Chairside tests are also referred to as office tests that require only simple and relatively less expensive equipment and can usually be performed with an acceptable degree of accuracy without highly expensive special training. In tests of this type, simplicity and rapidity are more important than accuracy and the results should be interpreted with this in mind. Positive findings should usually be confirmed before the patient is told of any abnormality. [1] The established screening test for oral squamous cell carcinoma is clinical examination with biopsy and histopathological assessment being as gold standard to confirm the diagnosis.

Chairside diagnostic aids in oral cancer

Vital staining [3]

A] Toluidine Blue

B] Methylene Blue

C] Lugol's Iodine

D] Rose Bengal

Cytopathologic studies [15]

A] Oral exfoliative cytology

B] Brush biopsy

C] FNAC

2. Light-based detection systems [12]

a. Chemiluminescence

b. ViziLite plus

c. VELscope

3. Biopsy [5]

VITAL STAINING

Vital staining is a procedure where certain living

cells take up dyes, which selectively stains some elements in the living cells like mitochondria, lysosome, lipid vesicles, etc.[3] **Indications**

» To highlight the potentially malignant oral lesions and conditions.

» To identify the early lesions which could be missed out on clinical examination.

» To outline the full extent of dysplastic epithelium or carcinoma prior to excision of lesion.

» Selecting biopsy site in premalignant lesions. [3]

TOLUIDINE BLUE (TB) STAINING

Toluidine blue (also called as tolonium chloride) is an acidophilic metachromatic dye that selectively stains the acidic tissue components (carboxylates, sulfates and phosphate radicals). Application of vital stains to detect early oral premalignant and malignant lesions was first reported by Neibel HH and Chomet B in 1964. [4]

Principle.

As the toluidine blue has the ability to bind the tissue where acidic component is more, it is based on the fact that dysplastic and neoplastic cells contain more amount of nucleic acid quantitatively than normal cells or tissue. Also, the intercellular canals are more wider in malignant epithelium than the normal epithelium, thereby enhancing the penetration of dye.For the intravital staining, 1% of toluidine blue is used. [4]

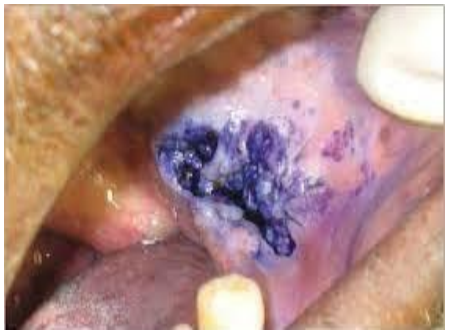

Figure 1 Toluidine blue staining

Procedure

Rinse the oral cavity twice with water for 20sec to remove food debris. Apply 1% of acetic acid for 20sec to remove ropey saliva and removal of glycoprotein and then apply 1% toluidine blue by using cotton swab or can be given as rinse. Then, rinse with 1% acetic acid is done to remove the mechanically retained stain in the oral cavity. Finally rinse the mouth with water. Then the colour change is assessed for the diagnosis as seen in **figure 1**. The interpretation is based on the colour change of suspected mucosa. Dark royal blue is considered as positive and light blue is doubtful while no colour uptake occurs is negative. [5]

Advantages

- It is inexpensive and simple procedure.
- Helpful for dentist to evaluate free surgical margins.

Disadvantages

- Both false positive and false negative results are more.
- Filiform papillae retain the dye due to more protein synthesis rate.
- Invaded underlying tissue does not take up the dye. So, the extent of submucosal spread is difficult to detect. [5]

LUGOL'S IODINE STAINING

Other names for Lugol's solution are I2KI (iodine–potassium iodide), strong solution (systemic), aqueous iodine solution. In 1929, Schiller W described Iodine test to delineate areas of cervical precancers. [6]

Principle

The principle is based on glycogen content of the cytoplasm and the reaction is known as the

iodine– starch reaction. Lugol's iodine solution is retained in normal squamous epithelial cells but not in dysplastic or malignant epithelial cells. Lugol's iodine solution produces a brown black stain by reaction of the iodine with glycogen. Normal mucosa contains higher amount of glycogen in comparison with abnormal mucosa and produces brown black stain. [6]

Procedure

Rinse with water/ carbocysteine syrup 250 mg/5 ml and dry with a cotton or gauze to clear the mucin layer. Then apply 3% Lugol's iodine until parakeratinized epithelium is stained a brown or black. **[fig.2]** After one to two minutes, interpret the stain reaction.[5]

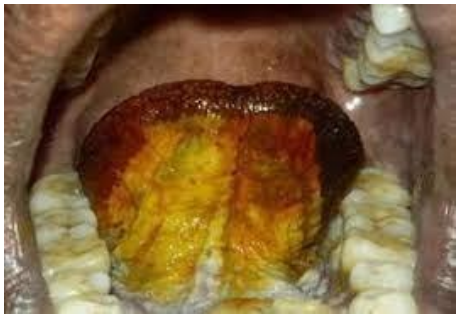

Figure 2 Staining with Lugol's iodine

Advantages

» It can be used for non-keratinized stratified squamous epithelium.

» Lugol iodine is cheaper, easy to use, widely available, and less time consuming.

Disadvantages

» It is an irritant that damages normal epithelial cells.

» Allergic reaction to iodine. [3]

METHYLENE BLUE

Methylene blue is a heterocyclic aromatic chemical compound. At room temperature it appears as a solid, odourless, dark-green powder, which yields a blue solution when dissolved in water. However, toluidine blue is hazardous if swallowed. Methylene blue is another recently proposed dye, which has all physiochemical structure similar to toluidine blue with the added advantage of being less toxic to the human body and cheaper and has recently been proposed for in vivo staining.**[figure 3]**The exact mechanism behind the uptake of methylene blue in the epithelial tissue may resemble that of toluidine blue. [7]

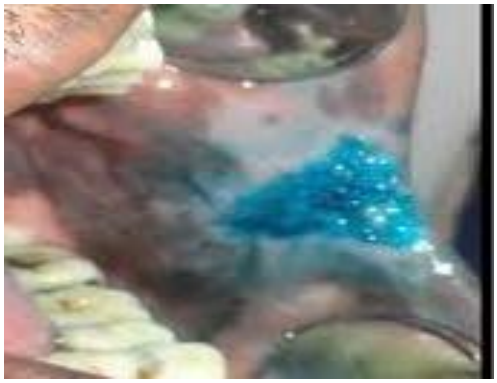

Figure 3 Methylene blue staining

ROSE BENGAL

Rose Bengal [RB] is the 4,5,6,7-tetrachloro-2',4',5',7'- tetraiodo-derivative of fluorescein molecule. RB staining is more widely used to diagnose ocular surface disorders. It stains desquamated ocular epithelial cells and the dead or degenerated cells, but not the healthy epithelial cells. Recently, a rose-bengal-conjugated with gold nano-rod platform was developed for the optical detection of cancerous cells.

ORAL CYTOLOGY

Oral Cytology has been widely accepted as a tool in the early diagnosis of cancer and precancer lesion which has gained popularity within a short period of time since its introduction by George Papanicolaou in 1942. The main concept behind cytological studieswas to study the cells, which are exfoliating due to pathologic or physiologic

process of thebody. [8]

Indications

» An oral lesion which cannot be identified with clinical certainty

» An oral lesion thought to be benign.

»To diagnose possible carcinoma in situ or less advanced premalignant lesion (dysplasia).

» An oral lesion strongly suggestive of cancer on a clinical basis. [8]

Figure 4 – Oral cytology

Procedure

Remove the debris from the lesion and scrapped the tongue blade firmly across the questionable area **[fig.4]**. Use a separate tongue blade soaked in its own container of water for each lesion smeared. Smear the collected cells evenly on a labelled glass slide. Immediately fix the slide by either: immersing it in 95 percent ethyl alcohol, or in equal quantities of 95 percent ethyl alcohol and ether; or by spraying it with commercial fixative Allow the slides to air-dryand send them to an oral or general pathologist for processing and evaluation.

The evaluation might be: [a] negative for cancer; (b) suspicious for cancer; or (c) positive forcancer. [9]

Advantages

» Painless, Bloodless, Non-invasive, Quick, Economical, Feasible and Requires minimum Armamentarium.

– Suitable for those patients with systemic disease who are contraindicated for the biopsy procedure.

» Useful for mass screening.

Disadvantages

» Relatively less information than histological slides

» Positive results are reliable but negative are not

» Suitable only for epithelial cells

» It is only an adjunct and additional aid but not a substitute for biopsy. [9]

BRUSH BIOPSY

OralCDx® brush biopsy is an oral transepithelial "biopsy" system that uses computer- assisted brushing. It consists of a method of collecting a trans-epithelial sample of cells from a mucosal lesion with representation of the superficial, intermediate and parabasal/basal layers of the epithelium.[10]

Procedure

A specially designed brush [fig.5] is used for epithelial cell collection and samples are eventually fixed onto a glass slide and stained with modified Papanicolaou test and analysed microscopically via a computer-based imaging system. Results are reported as "positive" or "atypical" when cellular morphology is a highly suspicious for carcinoma or epithelial dysplasia. Results are defined as negative when no abnormalities can be found. [15]

Fig. 5 Brush biopsy

Advantages

» Simple, rapid and non-aggressive.

» Relatively painless.

Disadvantages

» Technique cannot be performed in place of surgical biopsy.

» No value in detecting mucosal changes that are not readily visible to the naked eye.[5]

FINE NEEDLE ASPIRATION CYTOLOGY

Aspiration is a means of obtaining material from body cavity or cystic space or a fluid containing lesion **[fig. 6]**. Fine Needle Aspiration Cytology is a method whereby cells are obtained from a lesion using a thin bore needle and smears are made for cytopathological diagnosis. This technique is based on the fact that tumour cells are less cohesive and are easily aspirated. Needles – 18, 21, 23 or 25 gauze used during FNAC procedure. [2]

The smears are categorized as follow

» Inadequate - No squamous cells are seen due to failure of aspiration. Only blood obtained.

» Atypical cells or no abnormal - Only benign cells seen.

» **Atypical but no malignant cells** - Slight to moderate cellular and nuclear enlargement, moderate to severe hyperchromatism and increased nuclear-cytoplasmic ratio seen.

» Malignant - Great variations in nuclear size, pleomorphism, hyperchromatism, abnormal nuclear-cytoplasmic ratio. [10]

Figure 6 Fine Needle Aspiration Cytology

Indications

» The major indication for FNA relates to diagnosis of either primary malignancy or metastatic disease.

» Differentiate benign from malignant tumours,

» Evaluate metastasis in suspected or enlarged lymph nodes,

» Diagnose multiple tumours,

Advantages

» Cost effectiveness,

» Rapid reporting and bedside diagnosis,

» Minimal physical and psychological discomfort,

Limitations

» False positive diagnoses can be caused by regenerative epithelial hyperplasia and squamous Metaplasia.

» False negative diagnoses can be due to faulty technique.[5]

CHEMILUMINESCENCE (VIZILITE]

Vizilite, a diagnostic tool for the detection of early oral cancer and precancer are based on theprinciple of chemiluminescence. The theory behind this technique is that the acetic acid removes the glycoprotein barrier and slightly desiccates the oral mucosa; the abnormal cells of the mucosa then absorb and reflect the white/blue light in a different way with the respect to normal epithelial cells. Hence normal mucosa appears blue, whereas abnormal mucosal areas reflect the light (due to more nuclear/ cytoplasmic ratio in epithelial cells) and appear a more acetowhite with brighter, sharper and more distinct margins.[10]

The kit contains 1% acetic acid solution, a capsule with an outer shell of flexible plastic and an inner vial is of fragile glass, and a retractor. Activation needs breakage of the glass vial by bending the

capsule. This allow the chemical products to react with it and produce a bluish- white light **[fig.7]**with a wave length of 430-580 nm that lasts for around 10 min. The procedure involves a one minute mouthwash with 1% acetic acid solution.[8]

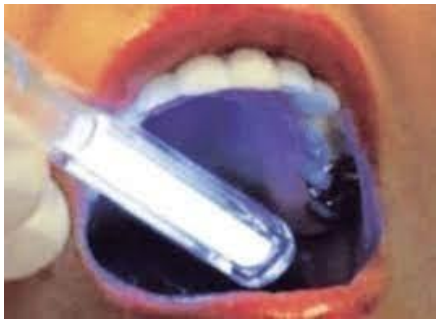

Figure 7. Vizilite

Indications

» It is used to diagnose leukoplakia and radiation mucositis.

» Identification of asymptomatic and clinically non-evident lesions.

» Diagnostic aid for the detection of oral cancer and premalignant early lesions.

Advantages

» Vizilite has the advantage in that it is capable of delineating the sharp borders between normal and abnormal oral mucosa and often extended beyond the clinically identified outline.

» Malignant lesions could be recognized without use of any adjunctive diagnostic tools. [11]

Tissue fluorescence imaging (VELscope)

Velscope system **[fig.8]** is a tissue fluorescence imaging system used for inspection of the oral mucosa. Under the intense blue light (400 to 600 nm wavelenght), normal oral mucosa emits a green autofluorescence, whereas abnormal areas absorb the fluorescent light and appear dark. Hence, early detection of pathological lesions is possible by detecting the early biochemical changes even before their evident appearance. [10]

Indication

» It is used for soft-tissue examination in the diagnosis of suspicious oral and surgicalborders.

Fig. 8 Velscope

Advantages

» The VELscope examination takes only 1-2 min and is painless and non-invasive, with no stains or rinses required.

» Possesses useful benefit in the determination of surgical borders and post-surgicalevaluations.

» It covers large surface area of the oral cavity.

» Small lesions can be identified easily.

Disadvantages

Prolonged and close tissue examination may cause patient discomfort.Equipment is costly. [11]

BIOPSY

The word biopsy originates from the Greek terms bios (life) and opsis (vision): vision of life. The technique allows us to give a proper histological characteristics of the suspected lesions, their differentiation, extent or spread of lesion, and to adopt an adequate treatment strategy.[12]

The aim of biopsy is to

» To define a lesion on the basis of its histopathological aspect;

» To establish a prognosis in a premalignant or malignant lesions;

» Contribute to the assessment of the efficacy of the treatment planning; 31

» Act as a document with a medico-legal value.

Indications of biopsy

» Any inflammatory lesion that does not respond to the treatment even after 2 weeks ofperiod.

» Any persistent hyperkeratotic lesion.

» Any lesion suspected as a neoplasm.

» Lesions of unknown aetiology, particularly when associated with pain, paraesthesia oranaesthesia.

» Inflammatory changes of unknown cause that persists for long periods. [12]

Contraindications of biopsy

» In those subjects with some systemic disorder that may worsen, or where secondarycomplications may occur.

»In difficult inaccessible area and in the very deep region where the surgical technique proves complicated or hazardous, with the risk of damage to neighbouring **Fig. 10 Punch biopsy**
structures.

» Suspected vascular lesions such as hemangioma, due to the risk of massive and persistent bleeding. [5]

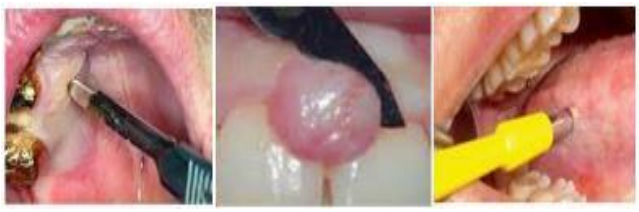

Figure 9 Incisional, Excisional and Punch biopsy

Types of biopsy [15] [Figure 9]

(A) Depending on the characteristics of the target lesion [15]

» Direct - located superficially, with easy access

» Indirect - when the lesion located in deep region and is covered by normally appearing mucosa or tissue

(B) The technique employed

» Excisional biopsy

» Incisional biopsy [14]

(C) The material used

» a conventional scalpel,

» a punch,

» B-forceps. [13]

(D) Purpose of the biopsy

Biopsies can be performed for

» Experimental purposes

» Diagnostic purposes. [13]

PUNCH BIOPSY:

Is a type of incisional biopsy where a special punch type of forceps is used for the removal of a tissue of the lesion **[fig. 10].** In this, a punch is held perpendicular to the lesion site and gently rotated with a firm downward pressure. Thus the punch is pushed downward till the subcutaneous fat is reached to it. The incised tissue in the punch is lifted and the pedicle is cut by using blade. The tissue is then carefully removed from the punch sent for histopathological examination.[5]

Fig. 10 Punch biopsy

Advantages:

Easy to perform and useful in mass screening program. Sutures may not be necessary if small diameter size punch is made and produce a more satisfactory specimen in bound down tissue.[15]

Drawbacks:

May not be adequate for biopsy of deeper pathology, difficult to biopsy in the freely mova 32 tissues (Eg: Soft palate, floor of mouth]

CONCLUSION:

Chairside investigations of oral cancer form an integral part of diagnosis and treatment planning. Hence investigations are very important in the diagnosis of various types of systemic diseases and precancerous and cancerous lesions. Various techniques of biopsies have been tried over the past and each method has its own pros and cons. Therefore, the clinician must choose the appropriate biopsy technique to arrive at a confirmatory diagnosis. Also treatment of any condition solely depends on the accurate diagnosis and thus histopathological diagnosis remains the gold standard.

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