

MICRONUCLEI IN SQUAMOUS CELL CARCINOMA

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Abstract:

Micronuclei are small chromatin bodies that appear in the cytoplasm by the condensation of acrocentric chromosomal fragments or by whole chromosome lagging behind the cell division. Micronuclei in oral exfoliated epithelial cells are widely used as a biomarker of chromosomal damage, genome instability and cancer risk in humans. In oral exfoliated cells these micronuclei are induced by variety of carcinogenic compounds, which have been suggested to be most common cause of premalignant lesion, conditions and oral cancer and thus can be used as a biomarker for cytogenetic damage. In this review, the formation of these important nuclear anomalies that are commonly seen in cancer and are indicative of genome damage that could increase the risk of developmental and degenerative diseases.

Keywords: Micronuclei; Oral squamous cell carcinoma; Exfoliative cytology; Fluorescence In Situ Hybridization(FISH).

INTRODUCTION

Micronuclei assay is potentially an excellent biomarker to detect chromosome loss or malfunction of mitotic spindle which is caused by aneugenic mechanism. This assay is a suitable internal dosimeter that allows to evaluate the biomarkers of DNA damage, cytotoxic effects, proliferative potential and cell death which are associated with ageing, neurovegetative disorders, high risk of cancer and the carcinogenic process which increases genetic instability (1). Micronuclei and other nuclear anomalies are the biomarkers of genotoxic events and chromosomal instability. The formation of these important nuclear anomalies that are commonly seen in oral cancer (2). The development of oral cancer is a multistep process arising from preexisting potentially malignant lesions. Oral squamous cell carcinoma accounts for 90% of all oral malignancies. Though diagnosis seldom presents difficulty, it is the cancer staging and histopathological grading that are important prognostication and micronuclei are good prognostic indicator. It is the nucleus that expresses the genotypic alterations caused in the process of malignancy (3).

In some human diseases, this desmosomal adhesion is disrupted and results in severe consequences for tissue integrity which causes blistering disorders. This review is focused on the adhesive function of desmosomes and the role of desmosomes in oral diseases.

MICRONUCLEI

Micronuclei are small extranuclear bodies that arise from acentric chromosome fragments or from whole chromosome that are excluded from the nucleus during mitotic cellular division (4) (Figure 1). Micronuclei are formed due to DNA breaks. During the cell division, the chromosome are drawn towards the two poles of the cell by spindle fibres. However, the breaks possess no centromere and hence spindle

fibres can not attach to them. These breaks remain outside the main nucleus and appear as small nuclei, which are known as micronuclei. Micronuclei and other nuclear abnormalities are the biomarkers of genotoxic events and chromosomal instability and are collectively measured in micronucleus cytome assay (5)



Figure 1 showing Micronuclei with chromosome fragments

ORAL CANCER

Oral cancer is the sixth most common cancer worldwide. More than 90% of all cancers are squamous cell carcinoma (SCC). The most important risk factors for oral cancer are use of tobacco or betel quid and the regular drinking of alcoholic beverages. The highest prevalence and incidence of oral cancer is found in Indian subcontinent where the risk of developing oral cancer is increased by the very prevalent habits of chewing tobacco, betel quid, and arecanut (6). All oral cancer are preceded by visible clinical changes in the oral mucosa usually in the form of white or red patch. Lack of public awareness about the signs, symptoms and risk factors, along with the absence of knowledge for early detection by health care providers are responsible for the diagnostic delay in identifying the potentially malignant disorders. Potentially malignant disorders is defined as the risk of malignancy being present in a lesion or condition either at the time of initial diagnosis or at a future date. Potentially malignant disorders are further classified into

- a) High risk -Erythroplakia, Leukoplakia, Oral Submucous fibrosis, Erosive lichen planus.

- b) Life style related - Tobacco keratosis, Reverse smokers palate, Actinic cheilitis.
- c) Infections - Candidiasis, syphilis
- d) Immunodeficiency - Solid organ transplantation, Graft versus host disease, Lupus erythematosus
- e) Inherited disorders - Xeroderma pigmentosum, Epidermolysis bullosa, Fanconi's anaemia (7).

epithelial surfaces by lightly scraping the surfaces, by swabbing, aspirating or washing the surfaces (10).

STAINS & STAINING CHARACTERISTICS

There are numerous staining methods out of which DNA specific stains are ideal for staining. Among them, the most widely used are Feulgen reaction followed by counterstaining with fast green to delineate cell cytoplasm (11). Acridine orange can also be applied with micronuclei frequency bright green and are distinguished from micronuclei like inclusions or contaminants. Micronuclei assay can also be performed by using the fluorescence in situ hybridization (FISH) is applied using a centromeric probe and propidium iodide for counterstaining. This method was considered to be effective than other stains for detecting degenerating other nuclear abnormalities (12).

ORAL CANCER – HISTOPATHOLOGICAL FEATURES

Oral squamous cell carcinoma (OSCC) is the 90% of all malignancies. The most important risk factors for OSCC are tobacco chewing, betel quid, areca nut, regular drinking of alcoholic beverages, smoking, sunlight exposure (6). Early OSCC often presents as a white patch, red patch or a mixed white and red lesion. With time superficial ulceration of the mucosal surface may develop. As the lesion grows it may become an exophytic mass with a fungating or papillary surface (8). OSCC is characterized by complex karyotypes that involve many chromosomal abnormalities, translocations and structural abnormalities, due to genotoxic exposure. Cells of this type of tumour often have errors in chromosome segregation that lead to the formation of lagging chromosomes or chromosome parts that become lost during the anaphase stage of cell separation and are excluded from the reforming nuclei. The laggards are observed in the cytoplasm of daughter cells as several secondary nuclei, which are smaller than the principal nucleus and are therefore called micronuclei (9). Exfoliative cytology is the reliable diagnostic tool in the diagnosis of presence or absence of malignancy.

MICRONUCLEI IN ORAL SQUAMOUS CELL CARCINOMA

Micronuclei is a small nucleus that forms whenever a chromosome or a fragment of a chromosome is not incorporated into one of the daughter nuclei during cell division. They are induced in cells by numerous genotoxic agents that damage the chromosome (13). Micronuclei assay is an excellent biomarker to detect chromosome loss or malfunction of mitotic spindle which is caused by aneugenic mechanism. This assay is a suitable internal dosimeter that allows to evaluate the biomarkers of DNA damage which are associated with ageing, neurovegetative disorders and a high risk of cancer. Oral cancer is the most common cancer among that 90% of all is SCC. The risk factors are smoking, tobacco chewing, betel quid, alcohol. One of the studies reported that the maximum number of cases with well-differentiated SCC were tobacco users. This can be explained on the basis of tobacco chewing habit in which the mucosa is in constant contact with the tobacco for a longer period causing DNA damage.

EXFOLIATIVE CYTOLOGY

Exfoliative cytology is the study of cells that have been shed or removed from the epithelial surface of various organs, the cells can be collected from the

Due to this DNA damage or chromosomal aberration these lagging in the mitotic cell division result in formation of micronuclei (14). Micronuclei is the nucleus that express the genotypic alterations caused in the process of malignancy. Moreover ,one of the study shows that micronuclei frequencies were found higher in SCC patients than in control subjects. Micronuclei frequencies were also found to be raised with histological grades of SCC. Micronuclei are induced in oral exfoliated cells by a variety of substances, including genotoxic agents ,betel nut, alcohol. Tobacco contain specific nitrosamines have been reported to be potent clastogenic and mutagenic agents which are thought to be responsible for the induction of chromosomal aberrations results in production of micronuclei (15). Therefore, micronuclei as a potential biomarker of oral squamous cell carcinoma.

CONCLUSION

Micronuclei assay is a sensitive, non-invasive and low cost technique that offers a very simple method for obtaining information on status of epithelial cells particularly DNA damage. The direct correlation between the micronuclei formation and genotoxic exposure makes the micronuclei assessment as an indicator of genomic damage. Hence, micronuclei analysis in oral exfoliated cells can be used as a biomarker to study genomic changes directly in target site affected by cancerous changes.

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