Original Article

# ONCEPTS OF BIPHASIC/BIMORPHIC LESIONS IN ORAL& MAXILLOFACIAL TUMORS

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## Abstract

Concepts of biphasic/bimorphic lesions in oral & maxillofacial tumors are not new in the field of histopathology.A biphasic/bimorphictumor is a truly histological term that denotes benign/malignant tissue which is characterized by the presence of two different cellular components. Various histogenetic theories have been suggested for the etiopathogenesisof biphasictumors. This review article focuses on some brief descriptions of histogeneticconcepts on the origin of biphasic tumorsand also categorized as well as summarized them.Categorization of biphasic tumorsdoes not exert any impact on their diagnosis, but it may affect in planning and effective management of these tumors, which is the aim of this review.

**KEYWORDS:** Biphasic tumors, Bimorphictumors, Histogenetic Theories

## INTRODUCTION

A tumor can be defined as a swelling of the tissue that does not imply a neoplasticprocess.Willis defined Neoplasm as an abnormal,uncontrolled,uncoordinated and persistent growth of tissue.[1]So, in the initial phase it is monoclonal or monophasic. But,as the tumor progresses, a series of molecular and genetic alterations advances the development and progression of these lesions.As a result, multiple mutations occur, which are essential for the formation of malignancy.Hence in advanced conditions, it converts into polyclonal and represents a complex heterogenous presentation.[2]In malignant tissue, two-cell populations are evident,due to which these tumors are called as Biphasic tumors.

So, **Biphasic Tumors**are those tumors in which tumor tissues are characterized by two-cell populations and both cells show malignancy in nature.[2]Whereas **BimorphicTumors**also represent two cell populations, out of which,one is neoplastic whereas the otherone is benign or non-neoplastic in nature.[2]Some of these group of tumorsof oral and maxillofacial regions includes MesenchymalChondrosarcoma, Carcinosarcoma of Salivary Gland,MelanoticNeuroectodermalTumor of Infancy, Epithelial-Myoepithelial Carcinoma, Spindle Cell Carcinoma and Nasopharyngeal Carcinoma – undifferentiated type.

## THEORIES OF BIPHASIC TUMORS[3]

**1. COLLISION THEORY**- According to this theory, two different malignant tissues collide and give rise to a biphasic tumor.[2,3]

2. **COMBINATION THEORY**- According to this theory,initially tumor arises from a single progenitor cell, but as the tumor progresses into its advanced condition,both components differentiate and give rise to a biphasic tumor.[2,3]

3.**CONVERSION THEORY**- According to this theory, originally tumor is a single cell population. But in the advanced stage, the second cell population originates from stromal reactions.[2, 3]

4.**COMPOSITION THEORY**- According to this theory,although a tumor originates from a stem cell,but at tumor progression, the first cell population gives arise to the second cell population. Hence biphasic tumor formed.[2,3]

A brief description of some tumors of the oral and maxillofacial region explains their biphasic nature:-

## CARCINOSARCOMA OF SALIVARY GLAND

Carcinoma-sarcoma of the salivary gland is a true malignant neoplastic condition that rarely occurs. It was first described by Kirklin et al in the year 1951 in the parotid gland.[4]Average age of 6 th -7 th decade of life with no sex predominance is reported in this aggressive salivary-gland malignancy.This salivary-gland neoplasm has both carcinomatous and sarcomatous counterparts, hence itfulfills the criteria of the biphasic tumor.Two thoughts have been proposed to explain the histogenesis of carcinosarcomas, namely the convergence and divergence hypothesis. The **convergence hypothesis** proposes thepolyclonal nature of stem cells, as the cause of tumorigenesis.[4]The **divergence hypothesis** suggests the monoclonal nature of tumorigenesis and it suggests that the origin of carcinosarcomas is from a single pluripotential stem cell that converts,later into epithelial and mesenchymal elements.[4]Ultrastructural studies also have explained that the histogenesis of the pleomorphic adenoma is from myoepithelial cells so, it could support the Conversion Theory, as an origin of the biphasic nature of this tumor.

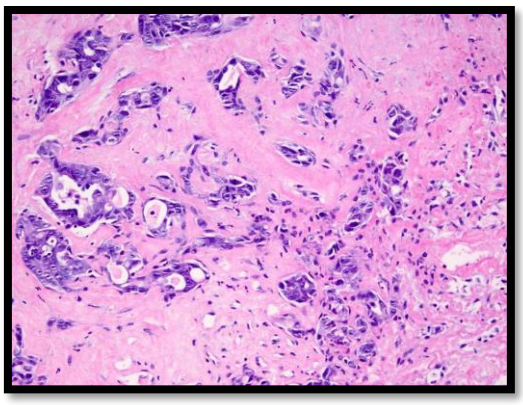

**Figure:1**[5]The carcinomatous component of a carcinosarcoma of Parotid Gland. In this case, it is poorly differentiated adenocarcinoma[5]

## MESENCHYMAL CHONDROSARCOMA

Mesenchymalchondrosarcoma (MC) is a malignant tumor of mesenchymal origin that shows biologically aggressive behavior with a poor survival rate[6] Itcommonly occurs in iliac bone, ribs, and long bones and adults are commonly affected with no sex predilection.[7]

Tumor'sbimorphic appearance shows both highly cellular undifferentiated tumor cells with an apparent small cell population transitioning into ovoid, spindle cells.As diagnosis by conventional histopathological examination is challenging, so the role of immunohistochemical analysis is quite important regarding this neoplasm. Immunohistochemical studies showed S-100 positivity. Although a two-cellular population is observed in mesenchymalchondrosarcomas, which are derived from a single cell lineage by **Combination Theory**, hence biphasic nature of this tumor is evident.

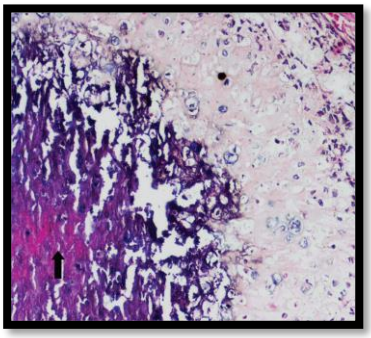

**Figure 2**[6]**:** Photomicrograph showing chondroid area along with ossification (H&E stain, ×100)[6]

### SPINDLE CELL CARCINOMA

Spindle cell carcinoma (SpCC) is an uncommon neoplastic aggressive and poorlydifferentiated type of squamous cell carcinoma,which usually occurs in the upper aero-digestive tract usually larynx (particularly vocal cords) and hypo-pharynx but oral-cavity is seldom involved.[8] This neoplasm generally occurs in males in the 6$^{th}$ to 7$^{th}$ decade of life with certain prognostic factors such as smoking,chronic alcohol

consumption,radiation and so on.In this neoplasm, both malignant epithelial as well as malignant mesenchymal components in the form of spindle cells are evident,hence it indicates a biphasic pattern.[2,8]
Theories of the origin of this biphasic tumor, includefirst theory is collision theory.[8]This theory explains both spindle cells and carcinomatous cells are originates from separate stem cells and in advance stages, both cells get combined and originate this tumor. Another theory advised the Composition theory.[2] Third theory supports the monoclonality of both spindle cells and epithelial cells and explains the driving force,due to which spindle cells are formed. Whereas fourth theory supports the de-differentiation of epithelial cells into spindle cells.

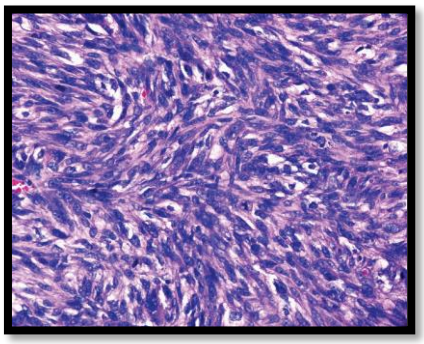

**Figure: 3[8]** Transition zone of the tumor", spindle-shaped tumor cells "dropping off" from SCC.

## MELANOTIC NEUROECTODERMAL TUMOR OF INFANCY

The melanoticneuroectodermaltumor of infancy is a not-so-common pigmented benign tumor that behaves aggressively.[9]Tumor of the infants which have no gender predilection and 3 to 6 months of age-groups infants affects usually.[9]Maxilla is most commonly affected however some cases of mandible, brain or skull are also reported.Microscopically the tumor was formed by two cellular types arranged in a rich connective-fibrous stroma.[3]In one aspect, epithelial-like cells are evident whichare arranged in small islands, outlining acinous or glandular structures. In another aspect, less differentiated neuroblast-like cells are seen, which resembleneuroblastomas, with a round hyperchromatic core, and a poorly visible cytoplasm.[9]Hence, it supports the Combination Theory,which explains the biphasic nature of this tumor.[3]

## EPITHELIAL-MYOEPITHELIAL CARCINOMA

Epithelial-myoepithelial carcinoma (EMC) is a true and high grade malignant mixedtumor of the salivary gland which is biphasic in origin as both the epithelial and stromal components fulfill the histological criteria of malignancy.[10] It represent the malignant counterparts of pleomorphic adenomas or benign mixed tumors[2]. It is generally composed of variable proportions of two cell types: An inner layer of duct liningcells and an outer layer of clear cells, which typically form double-layered duct-like structures. Clear cells, which are of myoepithelial origin, often predominate in number.[10]Two theories are found behind the origin of this malignant tumor-the convergence hypothesis, supports the origin of carcinosarcomas is from two or more stem cells, hence polyclonal nature of this tumor is evident. Other theory is the divergence hypothesis which supports the monoclonal nature of tumorigenesis,because according to this theory,carcinosarcomasarise from a single totipotent stem cell which later-on differentiates into separate epithelial and mesenchymal components.[3]So, the "driving force" behind the convergence theory while the divergence hypothesis supports the combination theory.

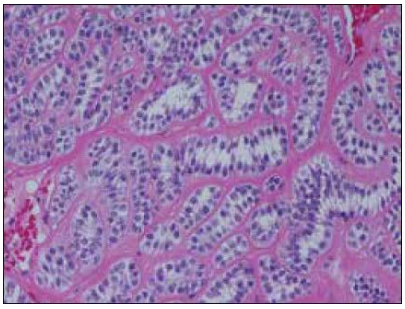

**Figure 4[10]**: Myoepithelial type arranged in sheets, nests and tubules surrounded by abundant homogenous, eosinophilic, hyalinizedstroma with small inconspicuous vessels.[10]

## CONCLUSION

In the process of origin of these biphasic tumors, the histogenetic concept is the most accepted theory, which states that, these biphasic tumorsarise from two cells component. Further molecular studies are always advised for the identification and categorization of these tumors, although identification through histologic patterns is easier for pathologists because of the presence of two cell populations. Changing the terminologies actually may not highlight diagnostic standards, but it may alter the therapeutic issues, and this will eventually help in defining and categorizing biphasic tumors of jaws.Further studies are advised for the determination of the exact etiopathogenesis behind the origin of these biphasic/bimorphictumors.

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