International Poster Journal IPJ of Dentistry and Oral Medicine

Int Poster J Dent Oral Med 2011, Vol 13 No 1, Poster 520

Odontogenic tumors – a saga of its genesis

Language: English

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Date/Event/Venue:
December 26-28, 2008
XVII National Conference of IAOMP
Kolkata, India

The earliest reports on odontogenic tumors date back to 1839 and in spite of researches over the decades the etiology and pathogenesis of this distinct group of jaw lesions is still incompletely understood. It is well established that odontogenic tumors arise from the epithelial and/or mesenchymal elements of the tooth forming apparatus and along with epithelial-mesenchymal interactions there are molecular and genetic alterations associated with the development and progression of odontogenic tumors (figure 1). Odonogenesis is a complex process which involves the interplay of several genes, growth factors, signalling molecules, transcription factors and, intra- and extra- cellular molecules (figure 2). Any aberrancy in this process is likely to lead to malignancy. It would not be wrong to agree that as the tooth develops though various stages, any dental follicle lost in the path of odontogenesis could give rise to variants of odontogeneic tumors (figure 3) with progressive development of odontogenic derivatives. These dental follicles could be un-erupted third molars, aberrant follicles, and/or supernumerary tooth germs. There are several genes which on aberrant expression may lead to arrest of odontogenesis at that particular stage (Figure 4). Anomalies like anodontia/oligodontia may result from defects in expression of Msx1, Lef1, BCOR, whereas supernumerary teeth with permanent dentition may be due to RUNX2 and trichodentoosseous syndrome results from Dlx3, all of which may be a potential source of odontogenic tissues. Also recently it has been proposed that various tumerogenic factors (initiators) and tumor promoting factors (supporters) all play a role in synchrony towards the genesis of odontogenic tumors(Table-1). It is important to understand that the odontogenic tumors arise from the odontogenic apparatus and the complex process involves several stages and factors. Thus we intend to outline the multi-step etiology and draw the future attention towards better understanding of odontogenic tumors.

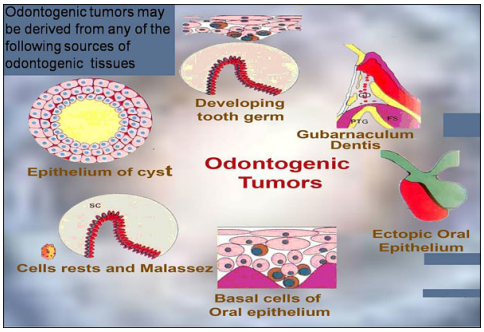


Fig. 1: Various histogenic sources for odontogenic tumors.

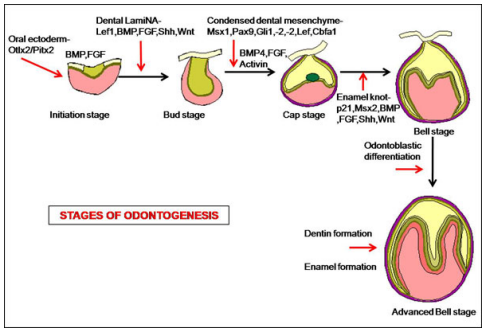
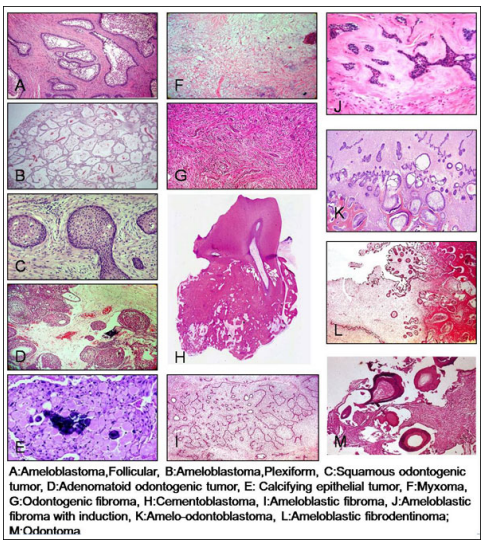


Fig. 2: Stages of odontogenesis, with expression of various genes and growth factors for each stage.



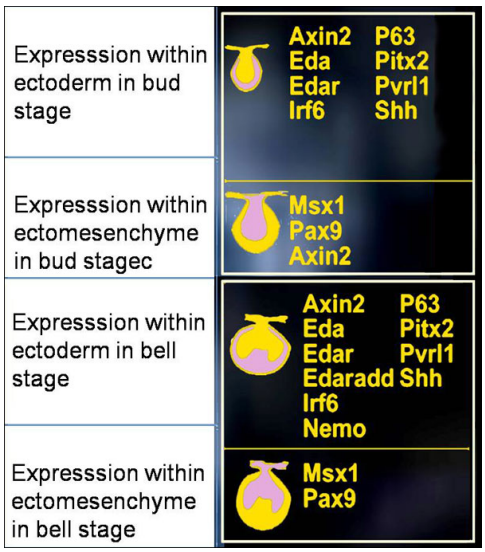


Fig. 3: Variants of odontogenic tumors

Fig. 4: Arrest of tooth development at bud to bell stage if corresponding genes are expressed aberrantly

TUMOR INITIATORS		
Oncogenes-	RAS, Cmyc, Fos	Dysregulation of cell proliferation
Tumor suppressor genes-	p53	cell cycle arrest
	APC	regulates Wnt pathway
	RTB	cell proliferation
Regulators of tooth development	SHH signalling	cell to cell interaction, cell proliferation, Epithelial Mesenchymal interaction
	Wnt signalling	nuclear accumulation of β-catenin
Oncogenes	EBV, HPV	
Hard tissue related proteins	bone sialoproteins, amelogenin	tumor development and progression; associated with pathologic mineralization
	BMP-2, -4, -7	
Growth factors	TGF-α,-β, FGF -1,-2	Tumor growth and invasion
	HGF	Cell differentiaton
Telomerase		cell immortality
Cell cycle regulators	cyclin D1, p61, p21, p27	Uncontrolled cellular division
Apoptosis related factors	Bcl-2, IAP, Fas, TNF-α, p53	Prolonged cell survival
TUMOR SUPPORTERS		
Cell adhesion molecules	E-selectin, ICAM-1, VCAM-1, E-cadherin, Integrin, CD44	Aid in tumor invasion and survival
Matrix degrading proteinases	MMP-1,-1,-1/ TIMP-1,-2, Heparanase	
Angiogenic factors	VEGF	
Osteolytic cytokines	IL-1, -6, TNF-α, PTHrP, RANKL/OPG	

Table 1: Tumor initiators and tumor supporters in pathogenesis of odontogenic tumors

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