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SHORT COMMUNICATION

ODONTOGENIC KERATOCYST – RECENT UPDATES IN MANAGEMENT

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ABSTRACT

Odontogenic keratocyst is one of the most aggressive odontogenic cysts arising from odontogenic epithelium. It can become quite large because of its ability for significant expansion, extension into adjacent tissues and rapid growth. Thus they are often locally destructive and tend to recur. The goals of treatment should eliminate the potential recurrence and minimize the surgical morbidity.

KEY WORDS: Keratocystic odontogenic tumor, Odontogenic keratocyst, Basal nevus syndrome, Marsupialization, Vismodegib

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INTRODUCTION:

The term "Odontogenic Keratocyst" was first suggested by Phillipsen in 1956[1]. Historically, the first reported case of a dental cyst was in 1774 by an anatomist, John Hunter. Since 1930s, many researchers noted that dental cysts could be found with keratinization in the lining of the cyst and keratin itself in the cyst contents. The general belief is that these cysts originate from remnants of the dental lamina. But in many cases, a tooth is generally present and, so, they are believed to originate from additional remnants of the lamina that are not involved in tooth formation. In a few cases, they may arise from the oral mucosa, due to the presence of daughter cysts. The basal cell nevus syndrome or the Gorlin-Goltz Syndrome is a genetic condition that includes a triad of Odontogenic Keratocyst of the jaws, skeletal abnormalities like bifid ribs, frontal bossing, and calcification of the falx cerebri and cutaneous manifestations such as basal cell carcinomas and palmar pitting of the hands[2].

RADIOGRAPHIC FEATURES:

Odontogenic Keratocyst present radiographically either as a unilocular or a multilocular radiolucency, occurring mostly in the posterior mandible. Expansion of the buccal and lingual plates occur late as it primarily tends to invade and spread along the marrow spaces[3].

PATHOLOGIC FEATURES:

The presence of keratin flakes or a protein level of less than 4 g per 100 ml in the sample obtained after aspiration biopsy are indicative of Odontogenic Keratocyst[4]. Odontogenic Keratocyst has a higher prevalence rate in the mandible than in the maxilla, with a ratio of 3:1. In the mandible, it occurs more often in the third molar area/ascending ramus when compared to the tooth-bearing area anterior to the third molar with a ratio of 3:2[5]. There are two variants of this pathology based on their histological appearance, one being Orthokeratinized and the other being Parakeratinized. Orthokeratinized OKC have a lesser recurrence rate when compared with the Parakeratinized OKC.

TREATMENT:

The conventional treatment for Odontogenic keratocyst has been primarily, enucleation of the lesion with peripheral ostectomy, followed by chemical cauterization. Chemical cauterization was done using Carnoy`s solution which has chloroform as a constituent. Due to the carcinogenic potential of chloroform, its use has been discouraged and a Modified Carnoy`s solution was advocated. It lacked the potency of Carnoy`s solution. Marsupialization, Cryotherapy, Radical resection[6] and Endoscopic enucleation[7] are also advocated based on clinical criteria. With the advancements in research, many newer trends have emerged in the management of this pathology. Ledderhof et al studied the usage of topical 5- Fluorouracil, an anti-metabolite in the place of modified Carnoy's solution after enucleation and peripheral ostectomy. There were no recurrences or adverse effects in the follow up period and a significantly lower incidence of inferior alveolar nerve paresthesia was observed. It was readily available, had technical ease, had shorter operating time, similar efficacy and had decreased morbidity compared to modified Carnoy`s solution[8]. Cases of Basal cell nevus syndrome are commonly associated with mutations in the PTCH1 gene. The hedgehog pathway gets activated by binding of Sonic hedgehog protein to its receptor, which diminishes the inhibitory effect of PTCH on Smoothened Protein (SMO), that inturn activates an intracellular cascade which results in the activation and nuclear translocation of Gli family transcription factors. These receptors promote cellular proliferation and survival.

FUTURE PERSPECTIVE:

Vismodegib is a new drug, which is a selective Hh pathway inhibitor blocks Hh signaling by binding to SMO and inhibiting the activation of downstream Hh target genes. Vismodegib (150mg) is orally administered once daily, is approved by the Food and drug administration (FDA) in 2012. It should be administered for at least 11 months[9]. Ally et al found that Vismodegib can shrink some KCOTs in patients with Basal Cell Naevus Syndrome, with a mean size reduction of 50%. Two patients had complete resolution of 1 or more KCOTs, with no enlargement of existing tumors, no recurrence in any case and no development of new lesions[10]. It costs about $360 per 150mg tablet, so may work up to $131000 for 1 year

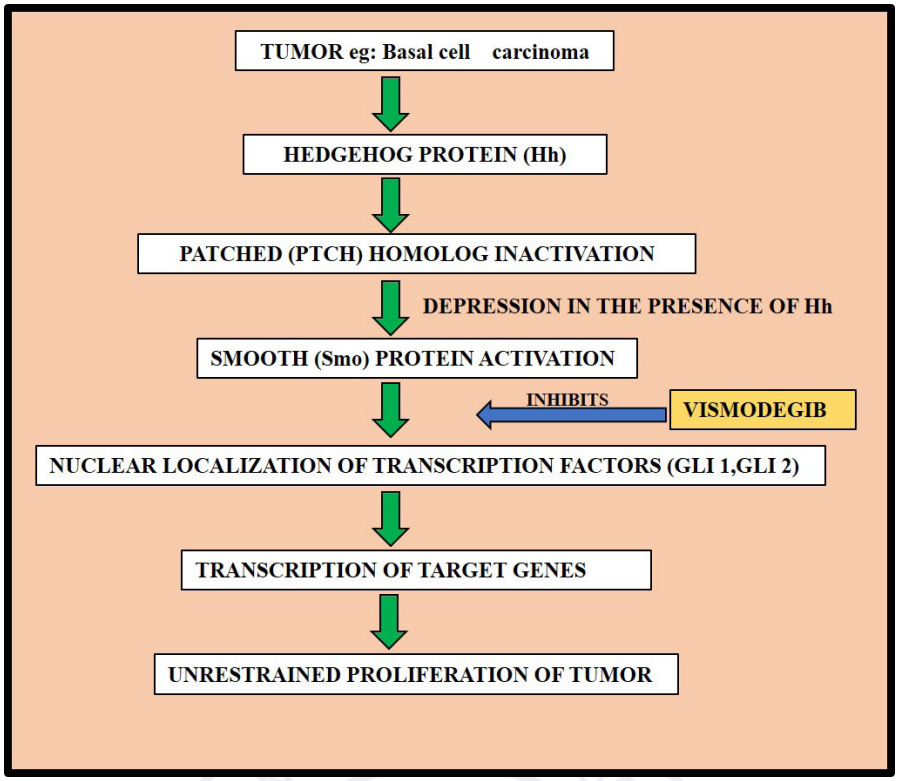

Fig 1- Site of action of Vismodegib

Schematic representation of hedgehog-signaling pathway: Hedgehog ligands bind to patched homolog 1, causing release of the suppression of smoothened by patched homolog 1. Smoothened interacts with suppressor of fused, which promotes glioma-associated oncogene transcription factor. Constitutive activation of smoothened protein plays a role in carcinogenesis. Vismodegib inhibits smoothened Protein

Jain et al reviewed Sonidegib, the second Hh signaling inhibitor approved by the FDA to treat Basal cell carcinoma following approval of the first SMO antagonist Vismodegib in 2012. Sonidegib interacts with SMO in the drug-binding pocket, where it acts as an antagonist, preventing downstream activation of Hh pathway signaling[11] (Fig 1). It costs upto $146000 for 1 year and can be given either orally or topically. Meticulous understanding of the pathogenesis of odontogenic keratocyst, along with a proper follow-up of the clinical trials of the recent advances, might provide us a better prognosis in cases that can be treated without surgery and to improve the patient's overall quality of life.

CONCLUSION:

Odontogenic keratocyst is amongst the numerous aggressive odontogenic cysts having significant recurrence rate. Numerous surgical strategies have been published such as decompression, marsupialization, enucleation with or without adjunct (Carnoy's solution, cryotherapy), as well as resection. Vismodegib can shrink some KCOTs in patients with Basal Cell Nevus Syndrome may offer an alternative to surgical patients. The obvious advantages of these treatment techniques are as follows:

- Eradication of the pathologic lesion
- Reduction of the potential recurrence
- Preservation of the continuity of the mandible, thus maintaining jaw function and shape

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Nil

CONFLICTS OF INTEREST:

There are no conflicts of interest.

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