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MINIREVIEWS

Clinicopathological and molecular insights into odontogenic tumors associated with syndromes: A comprehensive review

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Abstract

The association between genetic syndromes and odontogenic tumors encompasses several entities, reflecting the intricate interplay between genetic factors and the development of these lesions. The present study aimed to comprehensively investigate the associations between genetic syndromes and odontogenic tumors. We delineated the diverse spectrum of syndromic connections, including key syndromes such as Gardner syndrome, Gorlin syndrome, Schimmelpenning syndrome, and others. Our findings underscore the clinical significance of recognizing odontogenic tumors associated with genetic syndromes as diagnostic indicators for early intervention. We advocate for multidisciplinary collaboration among clinicians, geneticists, and researchers to deepen our understanding of the underlying mechanisms driving these syndromic associations. In light of this, our study contributes to the growing body of knowledge in dentistry and medical genetics, offering insights that may inform clinical practice and enhance patient care for individuals affected by genetic syndromes and odontogenic tumors.

Key Words: Genetic syndrome; Odontogenic tumors; Head and neck tumors; Misdiagnosis; Genetic mutations

Core Tip: It is important for the health professional to know that some odontogenic tumors have a close relationship with some genetic syndromes. Knowledge of this relationship can help a correct diagnosis and comprehensive treatment of the patient. Thus, the aim of the present review was to comprehensively investigate the associations between genetic syndromes and odontogenic tumors.

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INTRODUCTION

Odontogenic tumors (OT) represent a heterogeneous group of lesions, ranging from non-neoplastic tissue malformations (*i.e.*, hamartomas) to tumors with varying degrees of malignancy and clinical implications. Although considered uncommon, they account for approximately 1% of all oral diagnoses[1,2]. This prevalence can vary according to geographic region, with higher incidence rates reported in countries located in Asia and Africa[3,4]. The origin of OTs is attributed to the proliferation of remnants of the soft and hard tissues that give rise to teeth; however, the exact pathogenesis of these tumors remains unknown[5].

Some cases of OTs associated with syndromes have been observed[6]. Although syndromes often do not directly relate to neoplastic development, their occurrence may indicate a relationship between genetic factors and the pathogenesis of OTs, thereby contributing to a more comprehensive understanding of these entities in the realm of oral pathology. Accordingly, the aim of the present review was to provide insights into the association or concurrent lesions of OT and genetic syndromes based on clinicopathological and molecular aspects.

GENETIC SYNDROMES AND ODONTOGENIC TUMORS

Hereditary aspects are associated with some head and neck tumors[7]. OTs can manifest in association with various syndromes (Table 1), predisposing individuals to the development of multiple tumors concurrently[8-10].

Gardner Syndrome (Familial Adenomatous Polyposis)

Gardner syndrome, a distinct subtype of familial adenomatous polyposis, is characterized by mutations in the *Adenomatous polyposis coli* (*APC*) gene[11]. The genetic link between Gardner syndrome and the *APC* gene, located on chromosome 5, specifically within band 5q21, was identified in research studies[12-14]. The *APC* gene functions as a tumor suppressor, producing a protein that regulates cell growth and ensures proper cell cycle timing[15]. In Gardner syndrome, mutations in the *APC* gene result in uncontrolled cell growth. Additionally, Gardner syndrome involves other genetic anomalies, including loss of DNA methylation, mutations in the *RAS* gene on chromosome 12, deletion of the *DCC* gene on chromosome 18, and mutations in the TP53 gene on chromosome 17.

Due to the genetic heterogeneity of Gardner syndrome, there can be diverse phenotypic expressions; however, the three primary features are multiple gastrointestinal polyps, osteomas, and soft tissue tumors[16]. This syndrome holds more historical than clinical significance today, as these extraintestinal growths are more closely associated with specific mutation locations in the *APC* gene rather than with familial patterns.

In terms of oral manifestations, individuals may present with osteomas, supernumerary teeth, impacted teeth, odontomas, and osteomyelitis[7,17]. Concerning OTs, several cases of compound odontomas located in the anterior maxilla or complex odontomas in the posterior mandible or anterior maxilla have been described in the literature[18-21]. Additionally, in 2018, Salti and coauthors[22] published a case involving a large odontogenic myxoma in a patient with Gardner syndrome, who also presented with multiple osteomas and a compound odontoma. Figure 1 illustrates a case of Gardner syndrome in a patient with multiple osteomas and an odontoma.

Interestingly, Preuss *et al*[23] conducted a systematic review addressing the prevalence of oral lesions associated with Gardner syndrome. Their investigation revealed that the syndrome could present with lesions localized in the proximity of the jawbones. Notably, unicystic ameloblastoma emerged as the most frequently reported lesion, documented in three cases.

Gorlin syndrome

Gorlin syndrome is a hereditary cancer syndrome inherited in an autosomal dominant manner[7]. This condition is caused by mutations in the patched gene, which encodes a transmembrane receptor responsible for recognizing sonic hedgehog signaling proteins[24,25]. The syndrome is characterized by the presence of numerous basal cell carcinomas, along with accompanying skeletal, ophthalmological, and neurological abnormalities[26]. A small proportion of patients may present with additional features such as hypertelorism, macrocephaly, and cleft lip and/or palate during childhood,

Table 1 Summarize findings of syndromic conditions and odontogenic tumors

Odontogenic tumor	Syndrome	Genetic alteration	General clinical condition
Odontoma	Gardner syndrome	Mutations in the *APC* gene	Multiple colorectal polyps and various types of tumors, both benign and malignant
	Otodental syndrome	Not yet established (chromosome 11q13 deletion syndrome)	Globodontia, sensorineural high-frequency hearing loss and ocular coloboma
Adenomatoid odontogenic tumor	Schimmelpenning syndrome	Postzygotic mutations in *RAS* genes	One or several nevus sebaceous with abnormalities of ocular, cardiac, skeletal, and nervous systems
	Attenuated familial adenomatosis polyposis	Mutations in the *APC* gene, with less common occurrences linked to mutations in the MUTYH gene	Hundreds or thousands of adenomatous polyps in the large bowel
Ameloblastoma	Gardner syndrome	Mutations in the *APC* gene	Multiple colorectal polyps and various types of tumors, both benign and malignant
	Gorlin syndrome	Mutations in the patched (PTCH) gene	Numerous basal cell carcinomas and accompanying skeletal, ophthalmological, and neurological abnormalities
	Schimmelpenning syndrome	Postzygotic mutations in *RAS* genes	One or several nevus sebaceous with abnormalities of ocular, cardiac, skeletal, and nervous systems
	Simpson-Golabi-Behmel syndrome	Mutations in a semi-dominant X-linked gene encoding Glypican 3	Pre- and postnatal overgrowth, distinctive facial anomalies, and abnormalities affecting internal organs, the skeleton, and occasionally, varying degrees of intellectual disability
	Williams syndrome	Deletion of genes on chromosome 7q11.23	Developmental delay, intellectual disability, a specific cognitive profile, unique personality characteristics, cardiovascular disease, connective tissue abnormalities, growth deficiency, endocrine abnormalities, and distinctive facies
Odontogenic myxoma	Gardner syndrome	Mutations in the *APC* gene	Multiple colorectal polyps and various types of tumors, both benign and malignant

APC: *Adenomatous polyposis coli*.

along with desmoplastic medulloblastoma. Furthermore, ovarian neoplasms, cardiac fibromas, mesenteric keratocysts, rhabdomyosarcomas, and meningiomas may also be observed in some cases[7].

The diagnostic criteria for Gorlin syndrome have evolved over time. Initially proposed by Evans *et al*[24] in 1993, the criteria were modified by Kimonis *et al*[27] in 1997 and later revised by Bree *et al*[28] in 2011. A diagnosis can be established based on one of the following: (1) One major criterion and genetic confirmation; (2) Two major criteria, or (3) One major criterion and two minor criteria. Specific criteria typically include the presence of multiple basal cell carcinomas, jaw keratocysts, and various skeletal, ophthalmological, and neurological abnormalities. It is important to highlight that a thorough medical and family history, along with a physical examination - including an assessment for dysmorphic features, skeletal abnormalities, and skin abnormalities - is essential in suspected cases of the syndrome[29].

In the gnathic bones, Gorlin syndrome is strongly associated with odontogenic keratocysts (OKCs)[30]. However, cases reporting individuals with Gorlin syndrome and ameloblastomas have been published in the literature, underscoring the diverse spectrum of syndromic associations, including those with OTs, and the potential for multifocal manifestations in affected individuals[31-33]. A systematic review by Atarbashi-Moghadam *et al*[6] summarizing syndromic conditions and ameloblastomas identified six cases of ameloblastoma associated with Gorlin syndrome. Interestingly, these cases demonstrated a female predilection and a tendency for maxillary involvement.

Careful clinical evaluation and genetic testing are essential to confirm the diagnosis and guide management strategies. Early intervention is crucial in preventing complications and improving patient outcomes. Comprehensive patient care often requires a multidisciplinary approach, involving dermatologists, geneticists, dentists, and other specialists to monitor and treat the diverse manifestations of this syndrome[34,35].

Schimmelpenning syndrome (Epidermal nevus syndrome)

Schimmelpenning syndrome, also known as epidermal nevus syndrome, is a rare congenital disorder characterized by the presence of epidermal nevi-patches of abnormal skin that typically appear as raised, warty, or thickened areas. These are often associated with cerebral, ocular, or skeletal defects[36,37]. Postzygotic mutations in *RAS* genes have been linked to the development and progression of this disorder[38].

In individuals with Schimmelpenning syndrome, abnormalities in the development of the jaws may occur, primarily presenting as multiple adenomatoid odontogenic tumors (AOT)[10]. A systematic review conducted by Neumann *et al* [39] identified synchronous OTs in two cases diagnosed with Schimmelpenning syndrome[40,41]. These cases presented with multiple odontomas and an AOT[40], with one case also exhibiting synchronous squamous OT[41].

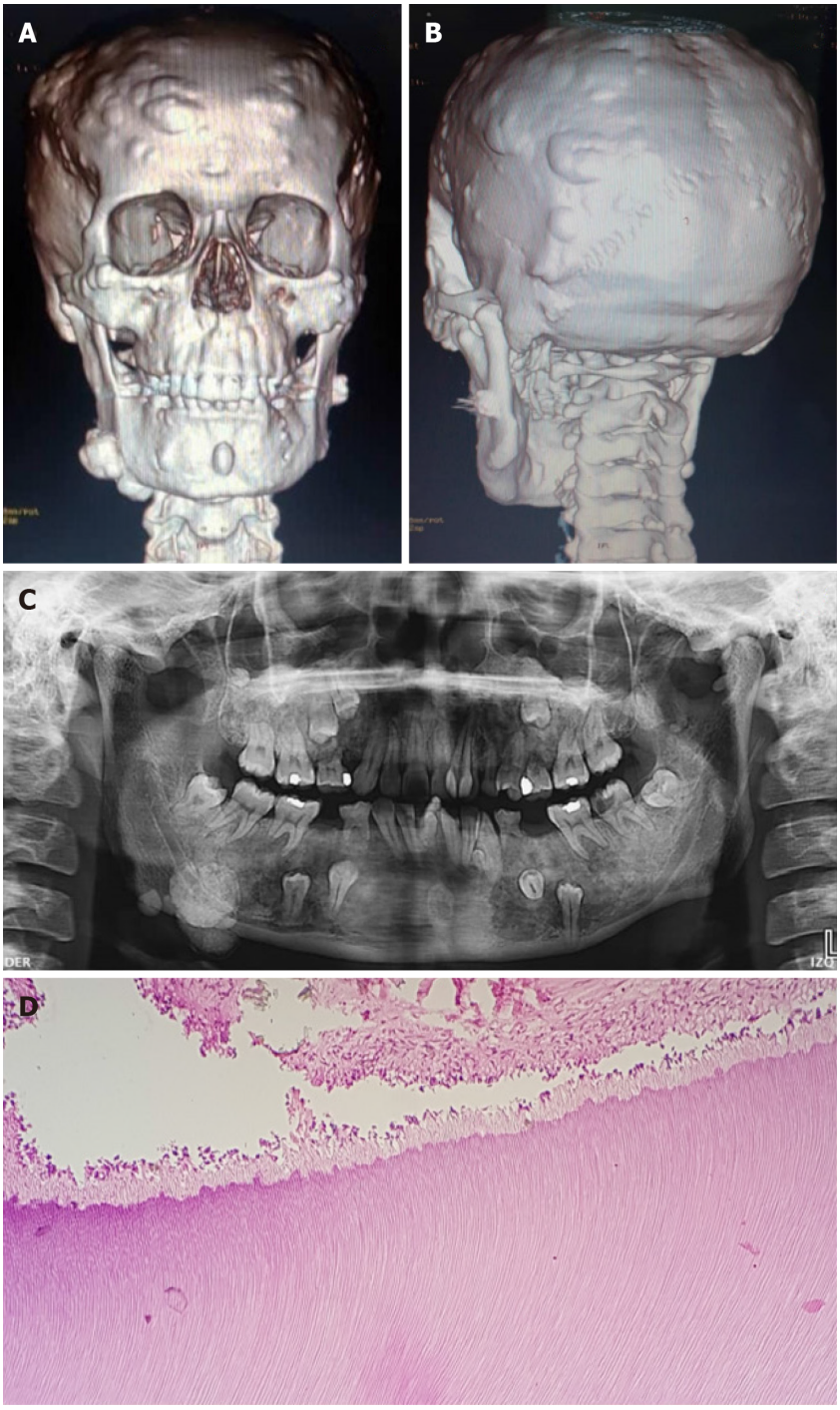

Figure 1 Gardner syndrome in a 22-years-female patient. A and B: Three-dimensional reconstruction images show multiple variable sized osteomas in craniofacial bones; C: Panoramic radiograph shows radiopacity in the right posterior region of the mandible diagnostic as odontoma; D: Haematoxylin and eosin staining section of the odontoma characterized by the presence of dentinal tubules, odontoblasts, and dental pulp.

Otodental syndrome

Otodental syndrome, also known as otodental dysplasia, features a distinctive dental condition called globodontia, often accompanied by sensorineural high-frequency hearing loss and ocular coloboma[42]. Although the specific gene associated with this syndrome remains incompletely elucidated, studies have indicated a deletion on chromosome 11q13 [43].

Interestingly, the dental characteristics alone can be definitive for diagnosis. The most consistent anatomical feature is the abnormal morphology of certain teeth[44]. This condition is marked by distinctive tooth fusion features, including abnormal bulbous enlargement of the crown, which appears spherical with poorly defined grooves[45]. Additionally, molars often exhibit taurodontism, characterized by an inverted crown-to-body ratio. There are also frequent alterations in the roots and pulp canals, making endodontic treatment unpredictable[45,46]. Other dental abnormalities associated with otodental syndrome include congenitally missing teeth and enamel hypoplasia[46]. Although few cases have been described, individuals with this syndrome may also exhibit a propensity for multiple odontomas[44,45,47].

Differential diagnoses for otodental syndrome include autosomal recessive sensorineural hearing impairment with dizziness and hypodontia, bilateral sensorineural hearing loss with multiple anterior dens invaginatus, and double dens invaginatus with developmental delay, progressive sensorineural hearing loss, and multituberculated mandibular incisors. For accurate diagnosis and management of the syndrome, a thorough medical, dental, and family history is crucial. An interdisciplinary approach is recommended.

Simpson-Golabi-Behmel syndrome

Simpson-Golabi-Behmel syndrome (SGBS) is a rare condition characterized by overgrowth and multiple congenital anomalies[48,49]. It results from mutations in a semi-dominant X-linked gene responsible for encoding Glypican 3 (GPC3). Information regarding the clinical and oral presentations of SGBS is limited in the literature. To the best of our knowledge, only one case of this syndrome associated with an OT has been reported[49]. The case involved a 16-year-old male who presented with multiple jaw lesions, including an OKC, ameloblastoma, lateral periodontal cyst, dentigerous cyst, and mucous retention cyst, affecting both the mandible and maxilla.

Williams syndrome

Williams syndrome results from the deletion of genes on chromosome 7q11.23, specifically involving the elastin gene. Since the initial description of the syndrome, understanding of the phenotype's complexity and its evolving characteristics has significantly advanced[50]. This includes insights into the genetic underpinnings, mechanisms driving specific phenotypes, and the benefits of various interventions. However, many questions remain unresolved, which limits the capacity to optimize care and enhance patient outcomes.

The syndrome is characterized as a multisystemic disorder, with diagnosis typically guided by the presence of indicative signs and/or symptoms[50]. Notable signs include supravalvular aortic stenosis, facial dysmorphisms, dental anomalies, neurodevelopmental delays, learning disabilities, and an excessively sociable demeanor[51]. The occurrence of OTs is exceedingly rare, with only one case of ameloblastoma reported thus far[52]. In this case, the authors suggest that further molecular and clinical studies are necessary to establish a definitive association between the syndrome and tumor development.

Attenuated familial adenomatous polyposis

Familial adenomatous polyposis (FAP) is a genetic disorder characterized by the development of at least 100 adenomas in the large bowel and various associated manifestations. It is inherited in an autosomal dominant manner and primarily arises from mutations in the *APC* gene, with less common occurrences linked to mutations in the *MUTYH* gene. A milder form, known as attenuated FAP, is characterized by the presence of fewer than 100 adenomas in the large bowel, distinguishing it from classical FAP. To date, only one case of an OT (specifically, an AOT) has been described in the literature in association with this syndrome[53].

CONCLUSION

This manuscript provides a comprehensive exploration of the intricate relationship between genetic syndromes and OTs. Our findings underscore the importance of recognizing the oral and maxillofacial manifestations associated with genetic syndromes, as these can serve as diagnostic clues for early detection and intervention. In this context, a thorough clinical examination is crucial. This should include a detailed patient history, consideration of underlying conditions, and relevant imaging tests. Additionally, understanding the associations between OTs and genetic syndromes helps clinicians identify patterns of presentation and anticipate potential complications or comorbidities. This knowledge can guide diagnostic workup, treatment planning, and long-term management strategies for affected individuals. Furthermore, it is important to note that while cases in the literature report OTs occurring in syndromic patients, the syndrome may not necessarily be associated with the etiopathogenesis of the neoplasm.

A significant aspect highlighted is the impact of missed diagnoses of genetic syndromes. Delayed or inaccurate identification can lead to suboptimal management and potentially worsen patient outcomes. For example, in Gardner syndrome, a delayed diagnosis may result in the progression of colorectal polyps to cancer and the development of jawbone lesions, which can lead to facial asymmetry, discomfort, and an increased risk of cancer. In the case of Gorlin syndrome, delays can lead to the progression of jawbone lesions and skin cancers, resulting in severe deformities, chronic pain, and more complex surgical needs.

We also emphasize the importance of incorporating genetic testing into clinical practice when a syndromic condition is suspected. Comprehensive genetic evaluations can not only confirm diagnoses but also provide valuable insights into the hereditary nature of these syndromes. Finally, managing OTs in syndromic patients requires a collaborative approach, involving researchers with expertise across the diverse conditions and genetic factors associated with each syndrome. This approach should consider both the specific characteristics of the tumor and the syndromic condition, aiming to provide optimal care, minimize complications, and enhance the overall quality of life for the patient.

Due to the nature of the study design employed, several limitations are evident. Firstly, the lack of a systematic search method meant that some relevant studies could not be included. Secondly, some case reports lacked the comprehensive details necessary to fully understand the syndrome and its association with OTs. Finally, the findings may not be universally applicable across all healthcare settings or populations due to variations in clinical practices and patient demographics.

FOOTNOTES

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REFERENCES

1 World Health Organization classification of head and neck tumours. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, editors. WHO Classification of Tumours, 4th Edition, Volume 9. Lyon: IARC Press, 2017
2 **Wright JM**, Soluk Tekkesin M. Odontogenic tumors: where are we in 2017 ? *J Istanb Univ Fac Dent* 2017; **51**: S10-S30 [PMID: 29354306 DOI: 10.17096/jiufd.52886]
3 **Sharma PN**, Ranka RK, Chaudhary MS, Gawande MN, Hande AH, Zade PF. Odontogenic tumors: A review of 93 cases in the Vidharba region of Maharashtra. *J Oral Maxillofac Pathol* 2020; **24**: 185 [PMID: 32508475 DOI: 10.4103/jomfp.JOMFP_145_19]
4 **Garg RK**, O'Connor MK, Sterling DA, Jacob L, Hammoudeh JA, Andrews BT. Pediatric Odontogenic and Maxillofacial Bone Pathology: A Global Analysis. *J Craniofac Surg* 2022; **33**: 870-874 [PMID: 34560739 DOI: 10.1097/SCS.0000000000008201]
5 **Bilodeau EA**, Hunter KD. Odontogenic and Developmental Oral Lesions in Pediatric Patients. *Head Neck Pathol* 2021; **15**: 71-84 [PMID: 33723756 DOI: 10.1007/s12105-020-01284-3]
6 **Atarbashi-Moghadam S**, Atarbashi-Moghadam F, Sijanivandi S, Mokhtari S. Ameloblastoma associated with syndromes: A systematic review. *J Stomatol Oral Maxillofac Surg* 2020; **121**: 146-149 [PMID: 31336213 DOI: 10.1016/j.jormas.2019.07.010]
7 **Nosé V**, Lazar AJ. Update from the 5th Edition of the World Health Organization Classification of Head and Neck Tumors: Familial Tumor Syndromes. *Head Neck Pathol* 2022; **16**: 143-157 [PMID: 35312981 DOI: 10.1007/s12105-022-01414-z]
8 **Kikuiri T**, Mishima H, Imura H, Suzuki S, Matsuzawa Y, Nakamura T, Fukumoto S, Yoshimura Y, Watanabe S, Kinoshita A, Yamada T, Shindoh M, Sugita Y, Maeda H, Yawaka Y, Mikoya T, Natsume N, Yoshiura KI. Patients with SATB2-associated syndrome exhibiting multiple odontomas. *Am J Med Genet A* 2018; **176**: 2614-2622 [PMID: 30575289 DOI: 10.1002/ajmg.a.40670]
9 **Ibituruna ACH**, Costa ARGF, Paulo LFB, Faria PR, Cardoso SV, Loyola AM. Multiple calcifying epithelial odontogenic tumor: case report and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2019; **128**: 268-272 [PMID: 31078504 DOI: 10.1016/j.oooo.2019.03.018]
10 **Nel C**, Uys A, Robinson L, van Heerden WFP. Multiple adenomatoid odontogenic tumours associated with eight impacted teeth. *Oral Radiol* 2021; **37**: 321-327 [PMID: 32770291 DOI: 10.1007/s11282-020-00471-w]
11 **Pereira DL**, Carvalho PA, Achatz MI, Rocha A, TardinTorrezan G, Alves FA. Oral and maxillofacial considerations in Gardner's syndrome: a report of two cases. *Ecancermedicalscience* 2016; **10**: 623 [PMID: 26981152 DOI: 10.3332/ecancer.2016.623]
12 **Neuman WL**, Wasylyshyn ML, Jacoby R, Erroi F, Angriman I, Montag A, Brasitus T, Michelassi F, Westbrook CA. Evidence for a common molecular pathogenesis in colorectal, gastric, and pancreatic cancer. *Genes Chromosomes Cancer* 1991; **3**: 468-473 [PMID: 1663781 DOI: 10.1002/gcc.2870030609]
13 **Nishisho I**, Nakamura Y, Miyoshi Y, Miki Y, Ando H, Horii A, Koyama K, Utsunomiya J, Baba S, Hedge P. Mutations of chromosome 5q21 genes in FAP and colorectal cancer patients. *Science* 1991; **253**: 665-669 [PMID: 1651563 DOI: 10.1126/science.1651563]
14 **Waller A**, Findeis S, Lee MJ. Familial Adenomatous Polyposis. *J Pediatr Genet* 2016; **5**: 78-83 [PMID: 27617147 DOI: 10.1055/s-0036-1579760]
15 **Ditonno I**, Novielli D, Celiberto F, Rizzi S, Rendina M, Ierardi E, Di Leo A, Losurdo G. Molecular Pathways of Carcinogenesis in Familial Adenomatous Polyposis. *Int J Mol Sci* 2023; **24** [PMID: 36982759 DOI: 10.3390/ijms24065687]
16 **Newman CA**, Reuther WL 3rd, Wakabayashi MN, Payette MM, Plavsic BM. Gastrointestinal case of the day. Gardner syndrome. *Radiographics* 1999; **19**: 546-548 [PMID: 10194797 DOI: 10.1148/radiographics.19.2.g99mr21546]
17 **Subasioglu A**, Savas S, Kucukyilmaz E, Kesim S, Yagci A, Dundar M. Genetic background of supernumerary teeth. *Eur J Dent* 2015; **9**: 153-158 [PMID: 25713500 DOI: 10.4103/1305-7456.149670]
18 **Kesharwani PN**, Tiwari R, Ramaiah A, Jairaj A, Anand R, Tiwari H. Multiple odontoma in Gardner syndrome: unusual report. *Int J Appl Dent Sci* 2018; **4**: 284-286
19 **Saito K**, Sekine M, Goto F, Yamamoto H, Kaneda S, Sakai A, Iijima H, Yamauchi M, Yamazaki A, Okami K. Gardner syndrome with odontogenic sinusitis: A case report. *Clin Case Rep* 2021; **9**: e04256 [PMID: 34194782 DOI: 10.1002/ccr3.4256]
20 **Antal G**, Zsigmond A, Till Á, Orsi E, Szanto I, Büki G, Kereskai L, Herbert Z, Hadzsiev K, Bene J. Case report: Initial atypical skeletal

symptoms and dental anomalies as first signs of Gardner syndrome: the importance of genetic analysis in the early diagnosis. *Pathol Oncol Res* 2024; **30**: 1611768 [PMID: 38807857 DOI: 10.3389/pore.2024.1611768]

21 **Zeng M**, Yao X, Pan Y, Gu H, Xiong F, Yin X, Wu B, Chen T. A novel APC mutation associated with Gardner syndrome in a Chinese family. *Gene* 2024; **896**: 148051 [PMID: 38043837 DOI: 10.1016/j.gene.2023.148051]

22 **Salti L**, Rasse M, Al-Ouf K. Maxillofacial Radiographic study of Gardner's syndrome presenting with odontogenic myxoma: A rare case report. *Stomatologija* 2018; **20**: 59-64 [PMID: 30531170]

23 **Preuss O**, Jaron A, Grzywacz A, Aniko-wlodarczyk M, Trybek G. The incidence and the type of stomatognathic disorders in patients with Gardner syndrome. A systematic review. *BJHPA* 2019 [DOI: 10.29359/bjhpa.11.4.14]

24 **Evans DG**, Ladusans EJ, Rimmer S, Burnell LD, Thakker N, Farndon PA. Complications of the naevoid basal cell carcinoma syndrome: results of a population based study. *J Med Genet* 1993; **30**: 460-464 [PMID: 8326488 DOI: 10.1136/jmg.30.6.460]

25 **Bresler SC**, Padwa BL, Granter SR. Nevoid Basal Cell Carcinoma Syndrome (Gorlin Syndrome). *Head Neck Pathol* 2016; **10**: 119-124 [PMID: 26971503 DOI: 10.1007/s12105-016-0706-9]

26 **Hasan A**, Akintola D. An Update of Gorlin-Goltz Syndrome. *Prim Dent J* 2018; **7**: 38-41 [PMID: 30428966]

27 **Kimonis VE**, Goldstein AM, Pastakia B, Yang ML, Kase R, DiGiovanna JJ, Bale AE, Bale SJ. Clinical manifestations in 105 persons with nevoid basal cell carcinoma syndrome. *Am J Med Genet* 1997; **69**: 299-308 [PMID: 9096761]

28 **Bree AF**, Shah MR; BCNS Colloquium Group. Consensus statement from the first international colloquium on basal cell nevus syndrome (BCNS). *Am J Med Genet A* 2011; **155A**: 2091-2097 [PMID: 21834049 DOI: 10.1002/ajmg.a.34128]

29 **Verkouteren BJA**, Cosgun B, Reinders MGHC, Kessler PAWK, Vermeulen RJ, Klaassens M, Lambrechts S, van Rheenen JR, van Geel M, Vreeburg M, Mosterd K. A guideline for the clinical management of basal cell naevus syndrome (Gorlin-Goltz syndrome). *Br J Dermatol* 2022; **186**: 215-226 [PMID: 34375441 DOI: 10.1111/bjd.20700]

30 **Silva LP**, Rolim LS, Silva LA, Pinto LP, Souza LB. The recurrence of odontogenic keratocysts in pediatric patients is associated with clinical findings of Gorlin-Goltz Syndrome. *Med Oral Patol Oral Cir Bucal* 2020; **25**: e56-e60 [PMID: 31880290 DOI: 10.4317/medoral.23185]

31 **Dalati T**, Zhou H. Gorlin syndrome with ameloblastoma: a case report and review of literature. *Cancer Invest* 2008; **26**: 975-976 [PMID: 19093254 DOI: 10.1080/07357900802039979]

32 **Eslami B**, Lorente C, Kieff D, Caruso PA, Faquin WC. Ameloblastoma associated with the nevoid basal cell carcinoma (Gorlin) syndrome. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008; **105**: e10-e13 [PMID: 18417377 DOI: 10.1016/j.tripleo.2008.01.034]

33 **Ponti G**, Pastorino L, Pollio A, Nasti S, Pellacani G, Mignogna MD, Tomasi A, Del Forno C, Longo C, Bianchi-Scarrà G, Ficarra G, Seidenari S. Ameloblastoma: a neglected criterion for nevoid basal cell carcinoma (Gorlin) syndrome. *Fam Cancer* 2012; **11**: 411-418 [PMID: 22565648 DOI: 10.1007/s10689-012-9529-3]

34 **Kiwilsza M**, Sporniak-Tutak K. Gorlin-Goltz syndrome--a medical condition requiring a multidisciplinary approach. *Med Sci Monit* 2012; **18**: RA145-RA153 [PMID: 22936202 DOI: 10.12659/msm.883341]

35 **Spadari F**, Pulicari F, Pellegrini M, Scribante A, Garagiola U. Multidisciplinary approach to Gorlin-Goltz syndrome: from diagnosis to surgical treatment of jawbones. *Maxillofac Plast Reconstr Surg* 2022; **44**: 25 [PMID: 35843976 DOI: 10.1186/s40902-022-00355-5]

36 **Amato C**, Elia M, Schepis C. Schimmelpenning syndrome: a kind of craniofacial epidermal nevus associated with cerebral and ocular MR imaging abnormalities. *AJNR Am J Neuroradiol* 2010; **31**: E47-E48 [PMID: 20299435 DOI: 10.3174/ajnr.A2062]

37 **Asch S**, Sugarman JL. Epidermal nevus syndromes: New insights into whorls and swirls. *Pediatr Dermatol* 2018; **35**: 21-29 [PMID: 29044700 DOI: 10.1111/pde.13273]

38 **Groesser L**, Herschberger E, Ruetten A, Ruivenkamp C, Lopriore E, Zutt M, Langmann T, Singer S, Klingseisen L, Schneider-Brachert W, Toll A, Real FX, Landthaler M, Hafner C. Postzygotic HRAS and KRAS mutations cause nevus sebaceous and Schimmelpenning syndrome. *Nat Genet* 2012; **44**: 783-787 [PMID: 22683711 DOI: 10.1038/ng.2316]

39 **Neumann BL**, Só BB, Santos LG, Silveira FM, Wagner VP, Vargas PA, Dos Santos JN, Mosqueda-Taylor A, Fonseca FP, Schuch LF, Martins MD. Synchronous odontogenic tumors: A systematic review. *Oral Dis* 2023; **29**: 2493-2500 [PMID: 36218070 DOI: 10.1111/odi.14401]

40 **Ernst LM**, Quinn PD, Alawi F. Novel oral findings in Schimmelpenning syndrome. *Am J Med Genet A* 2007; **143A**: 881-883 [PMID: 17366580 DOI: 10.1002/ajmg.a.31663]

41 **Chaves RRM**, Júnior AACP, Gomes CC, de Castro WH, Gomez RS. Multiple adenomatoid odontogenic tumors in a patient with Schimmelpenning syndrome. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2020; **129**: e12-e17 [PMID: 31402313 DOI: 10.1016/j.oooo.2019.06.006]

42 **Bloch-Zupan A**, Goodman JR. Otodental syndrome. *Orphanet J Rare Dis* 2006; **1**: 5 [PMID: 16722606 DOI: 10.1186/1750-1172-1-5]

43 **Kim YS**, Kim GH, Byeon JH, Eun SH, Eun BL. Chromosome 11q13 deletion syndrome. *Korean J Pediatr* 2016; **59**: S10-S13 [PMID: 28018436 DOI: 10.3345/kjp.2016.59.11.S10]

44 **Liu A**, Wu M, Guo X, Guo H, Zhou Z, Wei K, Xuan K. Clinical, pathological, and genetic evaluations of Chinese patient with otodental syndrome and multiple complex odontoma: Case report. *Medicine (Baltimore)* 2017; **96**: e6014 [PMID: 28151902 DOI: 10.1097/MD.0000000000006014]

45 **Su JM**, Zeng SJ, Ye XW, Wu ZF, Huang XW, Pathak JL. Three years of follow-up of otodental syndrome in 3-year-old Chinese boy: a rare case report. *BMC Oral Health* 2019; **19**: 164 [PMID: 31345197 DOI: 10.1186/s12903-019-0860-z]

46 **Paglia M**, Severino M, Gatto R, Giani G, Caruso S. Otodental Syndrome. *Eur J Paediatr Dent* 2023; **24**: 247-249 [PMID: 37668456 DOI: 10.23804/ejpd.2023.24.03.03]

47 **Beck-Mannagetta J**, Müller H, Richter E, Donath K. [Odontomas and pan-tonal hearing loss in the otodental syndrome]. *Dtsch Zahnarztl Z* 1984; **39**: 232-241 [PMID: 6585292]

48 **Tenorio J**, Arias P, Martínez-Glez V, Santos F, García-Miñaur S, Nevado J, Lapunzina P. Simpson-Golabi-Behmel syndrome types I and II. *Orphanet J Rare Dis* 2014; **9**: 138 [PMID: 25238977 DOI: 10.1186/s13023-014-0138-0]

49 **Kaya GŞ**, Özalp Ö, Özbudak İH. Synchronous occurrence of multiple distinct jaw lesions in Simpson-Golabi-Behmel Syndrome: A case report. *J Stomatol Oral Maxillofac Surg* 2019; **120**: 483-488 [PMID: 30553040 DOI: 10.1016/j.jormas.2018.12.001]

50 **Kozel BA**, Barak B, Kim CA, Mervis CB, Osborne LR, Porter M, Pober BR. Williams syndrome. *Nat Rev Dis Primers* 2021; **7**: 42 [PMID: 34140529 DOI: 10.1038/s41572-021-00276-z]

51 **Twite MD**, Stenquist S, Ing RJ. Williams syndrome. *Paediatr Anaesth* 2019; **29**: 483-490 [PMID: 30811742 DOI: 10.1111/pan.13620]

52 **Tuncer FB**, Sacak B, Akdeniz ZD, Celebiler O. Ameloblastoma in a Patient With Williams Syndrome and Use of Fibular Flap. *J Craniofac*

Surg 2017; **28**: e241-e242 [PMID: 28468204 DOI: 10.1097/SCS.0000000000003449]

53 **Marrelli M**, Pacifici A, Di Giorgio G, Cassetta M, Stefanelli LV, Gargari M, Promenzio L, Annibali S, Cristalli MP, Chiaravalloti E, Pacifici L, Tatullo M. Diagnosis and treatment of a rare case of adenomatoid odontogenic tumor in a young patient affected by attenuated familial adenomatosis polyposis (aFAP): case report and 5 year follow-up. *Eur Rev Med Pharmacol Sci* 2014; **18**: 265-269 [PMID: 24488918]

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