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The incidence and the type of stomatognathic disorders in patients with Gardner syndrome. A systematic review

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Keywords

Gardner Syndrome, oral lesions, cancer

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REVIEW

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Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Conclusions: This review provides evidence for associating FAP with oral disorders. Dentists can be the first doctor able to diagnose Gardner syndrome and refer patients for systemic treatment. The incidence of changes in the oral cavity is significant and should be considered as an indication of Gardner syndrome.

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INTRODUCTION

Diseases of genetic origin often manifest themselves as disorders of the stomatognathic system. Syndromes associated with dental disorders include familial adenomatous polyposis (FAP), Gardner syndrome (GS), Peutz–Jeghers syndrome (PJS), Cowden syndrome (CS), and Gorlin-Goltz syndrome (also known as nevoid basal-cell carcinoma syndrome (NBCCS)). Gardner syndrome, discovered by a college teacher of genetics Eldon J. Gardner, is defined as a triad of intestinal polyposis, various soft tissue tumors such as fibromas, lipomas, neurofibromas, and epidermoid cysts, and multiple osteomas, especially of the skull [1].

Gardner Syndrome (GS) is a variant of familial adenomatous poliposis (FAP), caused by the mutation of the APC (adenomatous polioposis coli) gene located on chromosome 5q22.2 (band q21 on chromosome 5) [1]. The APC gene is also known as a tumor suppressor gene. This hereditary syndrome is an autosomal dominant variant of FAP. 20% of patients represent spontaneous mutations with no family history [2].

In 1951, Gardner discovered a significant correlation between the external osseous, cystic tumors and polyposis coli, which was followed by the first description of the syndrome in 1953 [3,4]. Gardner syndrome affects 10%-50% of patients with FAP [5] with a prevalence of 1:8000 to 1:1400 [6,7], and is the most common gene mutation in colorectal cancers [8,9]. The incidence of GS in the general population has been estimated at 1:14,025 live births. Gardner syndrome affects multiple systems [2]. It is accompanied by diarrhea, rectal bleeding, anemia and abdominal pain, caused by the presence of intestinal polyps, with a 100% likelihood of malignant transformation [10].

Malignant transformation of colorectal polyps is characteristic for patients under 40 years of age [5] while other symptoms occur in the second decade of life [4]. Symptoms are usually present by the end of the second decade of life, but they may appear anytime between two months and 70 years. In spite of colorectal cancers, GS is characterized by numerous extra-intestinal lesions like dental abnormalities. Over 30% of patients suffering from Gardner syndrome suffer from dental disorders. Most frequently reported ones include:

- supernumerary teeth
- impacted teeth
- congenitally missing teeth (hypodontia)
- root abnormalities
- dentigerous cysts
- complex and compound odontomas
- taurodontism
- hypercementosis
- osteomas
- epidermoid cysts
- enostoses [1–45].

According to literature, the most common regions affected with supernumerary and impacted teeth are the incisor and premolar regions. Supernumerary teeth have a different shape: e.g. they are tubercular or peg–shaped. The localization of odontomas is similar to tooth abnormalities and the most common odontomas are compound. Osteomas cause expansion of the jaw bones and very often can be palpable through oral mucosa or the skin or even clinically visible. They are usually asymptomatic, very often cause disfigurement, asymmetry, and limited or

or decreased function. Osteomas are most commonly found in the skull, mandible, facial bones and paranasal sinuses [10].

Treatment of patients with Gardner syndrome should be conducted in consultation with orthodontists. Osteomas should be surgically removed, but impacted asymptomatic teeth can be left without surgical treatment [12]. Gardner syndrome can be initially diagnosed by a dentist; early diagnosis should be important and play an essential role. The most important for diagnosis is the triad of signs: intestinal polyposis, bony tumors, and soft-tissue lesions [3]. The aim of this study was to review dental disorders are associated with GS. To diagnose GS, panoramic radiography should be used for the early detection, but this examination also has its limitations. In case of doubts during diagnosis, cone beam computed tomography (CBCT) should be performed.

The aim of this study was to determine the prevalence of oral lesions associated with Gardner syndrome based on the available literature.

MATERIAL AND METHOD

The selecting and screening process is shown in Fig. 1.

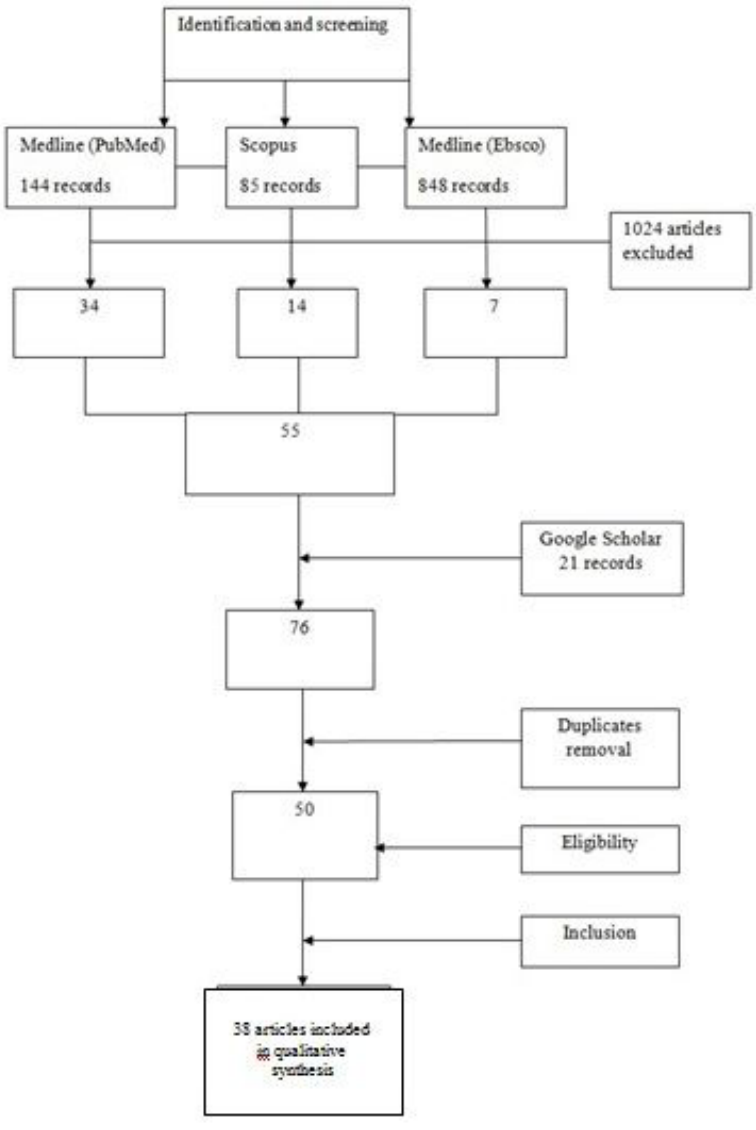

Fig. 1. Screening process

Medline (Ebsco), Scopus, Google Scholar and Medline (PubMed) databases were searched using the equation: ("gardner syndrome"[MeSH Terms] OR ("gardner"[All Fields] AND "syndrome"[All Fields]) OR "gardner syndrome"[All Fields]) AND ("mouth"[MeSH Terms] OR "mouth"[All Fields] OR "oral"[All Fields]). A total number of 1077 results were selected. Inspection of the abstracts was performed by two independent researchers. Articles which were not written in English and lacked information about oral lesions were excluded from the study. Forty-seven articles were finally selected from the databases for this study.

RESULTS

A total number of 38 articles were selected for this study. Because of the infrequency of Gardner Syndrome, there were no systematic reviews or clinical trials associated with GS. This was the reason behind only including case reports in the study. The results of qualitative synthesis are shown in Table 1 and Table 2. The first table includes tooth disorders, root abnormalities, ostemomas, enostoses, hamartomic lesions – odontomas. Table 2 consists of types of odontogenic tumors which are associated with Gardner syndrome.

The case studies involved 56 patients. The majority of changes connected with Gardner Syndrome were osteomas, found in 37 cases. The prevalence was similar in both the maxilla and mandible. Tooth impaction was found in 31 patients. The average age of the patients was 29.4 years. The patient with the highest number of impacted teeth [13] was a 37 year old man. Gardner syndrome can also be associated with lesions localized around the jaw bones. The most often mentioned lesion in literature was a unicystic ameloblastoma, which occurred in three patients (Table 2).

Table 1. Lesions associated with Gardner syndrome

Disorder	Region/tooth number	Age/sex	Methods	References
Odontoma	1) 11	-	OPG	3
	2) Reg. 33 and 45	37/male	OPG	16
	3) Reg. 44	19/male	OPG	18
	4) Multiple	25/female	OPG	21
	5) Reg. 15	33/female	OPG,CT	2
	6) Multiple	22/female	OPG,CBCT	10
	7) Maxilla	24/female	OPG/CBCT	10
	8) Multiple	25/female	OPG	22
	9) Maxilla	30/male	OPG/CBCT	15
	10) Reg. 22	17/female	OPG	8
	11) Mandible	19/male	OPG	23
	12) Multiple	31/female	OPG	18
Super-numerary teeth	1) 11,15,23	52/male	OPG, CT	14
	2) 29	37/male	OPG	16
	3) 24,19	37/male	OPG	17
	4) 15,23,29,45	22/male	OPG	4
	5) 11	9/female	OPG	18
	6) 22	17/female	OPG	19
	7) 36	31/female	OPG,CBCT	20
	8) 45,33,35	12/female	OPG	21
Impacted teeth	1) 11,15,23,34,35,45	52 /male	OPG,CT	14
	2) 43,13	47/male	OPG	16
	3) 18,28,38,48,33,34	17/male	OPG	17
	4) 13,23,38,32	44/male	OPG	25
	5) 13	55/male	OPG	26
	6) 13, 15, 18, 23, 33,34,35,3,44,45,48	46male	OPG, CBCT	13
	7) 11, 12, 13, 33, 21, 22, 45, 27, 29	37/male	OPG	15
	8) 15,14,25,35,34,44,45	19/male	OPG	6
	9) 15,14,23,43,44	19/male	OPG	21
	10) 18,14,15,11,21,24,25,35,34,33, 43,44,45	37/male	OPG	17
	11) 18	7/male	OPG	27

Table 1 – continued

Disorder	Region/tooth number	Age/sex	Methods	References
Impacted teeth	12) 15,23,45	22/male	OPG	4
	13) 15,23,25,34,45	25/female	OPG	22
	14) 23,24,25,33,34,35,44	33/female	OPG	2
	15) 23,33	24/female	OPG,CBCT	10
	16) 18,15,14,13,21,22,23,24,28,35, 33,32	23/female	OPG,CBCT	10
	17) 13,25,45	22/female	OPG,CBCT	10
	18) 13,21,25	21/female	OPG,CBCT	10
	19) 13,23,43	22/male	OPG,CT	28
	20) 25,35,34,36,37,38	38/female	OPG	29
	21) 33,38	25/female	OPG	22
	22) 14,15,24,25,34,35,33 43,44,45	21/male	OPG	30
	23) 13,23,14,15,24,25,45 44,43,35,34	24/female	OPG	30
	24) 44	10/male	OPG	18
	25) 13,43	28/male	OPG	31
	26) 33,45	12/female	OPG	20
	27) 21,23	25/female	OPG	32
	28) 15,23,34,45	45/male	OPG	33
	29) 13,33	30/male	OPG,CBCT	15
	30) 11,12,21,22,32,42,43	15/male	OPG/CBCT	34
	31) 13,21,22,33	66/male	OPG,CBCT	34
Root abnormalities	1) 46,47 resorption	52 /male	OPG,CT	14
	2) Taurodontism: 36,37,46,47,48	45/male	OPG	6
Osteomas	1) 11,38 reg.	-	OPG	3
	2) Multiple	20/male	OPG, CT	5
	3) Multiple: maxilla and mandible	47/male	OPG	5
	4) Mandible	17/male	OPG	5
	5) Condyle	16/male	OPG	35
	6) Angle, ramus and at the inferior border of the mandible.	20/male	OPG	36
	7) Multiple: maxilla and mandible	55/male	OPG	26
	8) Multiple: mandible and condyle	46/male	OPG,CT	13
	9) Maxilla and angle of mandible	20/male	OPG,CT	13
	10) Angle of mandible	37/male	OPG	15
	11) Mandible	19/male	OPG, CT	37
	12) Angle of mandible	19/male	OPG	20
	13) Mandible	64/female	OPG	38
	14) Maxilla and mandible, condyle	37/male	OPG,CT	17
	15) Mandible	7/male	OPG	27
	16) Mandible	22/male	OPG,CT	4
	17) Maxilla	66/female	OPG	39
	18) Mandible and maxilla	33/female	OPG,CT	2
	19) Angle of mandible and region of apices of mandibular right molars	29/male	OPG	7
	20) Angle and body of mandible, anterior part of maxilla	24/female	OPG,CBCT	10
	21) Angle and body of mandible, anterior part of maxilla	23/female	OPG,CBCT	10
	22) Angle of mandible, maxilla	22/female	OPG,CBCT	10
	23) Angle of mandible, maxilla	21/female	OPG,CBCT	10
	24) Anterior region of mandible	22/male	OPG,CBCT	27
	25) Multiple – body, ramus of mandible	38/female	OPG	29
	26) Body and angle of mandible	25/female	OPG	23
	27) Anterior region, ramus, angle of mandible	21/male	OPG	15
	28) Maxilla	24/female	OPG	30
	29) Mandible	10/male	OPG	18
	30) Mandible body	31/female	OPG,CBCT	19
	31) Corpus of maxilla, angle of mandible	27/male	OPG,CT	40
	32) Body of mandible	28/male	OPG	31
	33) Body of mandible	25/female	OPG	32
	34) Maxilla and mandible	45/male	OPG	33
	35) Maxilla	30/male	OPG,CBCT	23
	36) Multiple: maxilla, mandible	26/male	OPG,CBCT	41
	37) Multiple: maxilla, mandible	66/female	OPG,CBCT	34
Enostoses	1) Maxilla and mandible	52/male	OPG,CT	14
	2) Mandible	10/male	OPG	18

Table 2. Odontogenic tumours associated with Gardner syndrome

Histopathologic diagnosis	Age/sex	Methods	References/ authors
KCOT (keratocystic odontogenic tumour)	62/male	OPG, HP	11
OOC (orthokeratinized odontogenic cyst)	62/male	OPG,HP	11
Ghost cell tumour	1) 62/male 2) 37/male	OPG, HP OPG, HP	11 15
Unicystic ameloblastoma	1) 19/male 2) 14/male 3) 15/female	OPG, HP OPG, HP OPG, HP	18 19 27
Ameloblastic carcinoma	37/male	OPG, HP	15
Dentigerous cyst	30/male	OPG,CBCT	45

DISCUSSION

The APC gene is known as a regulator of epithelial behavior and tissue architecture [9]. It is also a tumor-supressor gene which degrades beta-catenin and inhibits its nuclear localization [8]. In the case of a lack of the suppressor gene, the beta-catenin-Wnt signaling is incorrectly and permanently activated. APC gene mutation is associated with colon cancer and familial ademato poliposis (FAP). Malignant changes of adenomas localized in the colon have a 100% potential rate. The age at which colon cancer occurs is 20–40 years [7]. Nearly 50% patients with this mutation has oral disorders such as osteomas, impacted and supernumerary teeth, which is called Gardner Syndrome.

Oral examination and dental treatment for patients with Gardner syndrome are very important elements of therapy. Sometimes diagnosis of the disease can be performed solely on the basis of dental abnormalities. Because of the 100% potential of colon cancer in patients with GS, dental examination in every patient should be conducted with accurate precision [3, 11, 14]. The most important and easiest part of this examination is radiography, with the orthopantomogram recommended as a routine diagnostic tool. Extending the diagnosis with a pantomographic picture should take place in case of any doubts about the condition of the patient's teeth. Importantly, the dentist can be the first person to recognize this syndrome, implement additional blood examinations and refer the patient to a general practitioner.

In literature there were only a few reports of Gardner Syndrome. The most common dental abnormalities associated with this syndrome are impacted teeth and osteomas. The high frequency of occurrence is also characterized by the presence of supernumerary teeth in the upper canine region. Dentigerous cysts, which are mentioned as a common disorder associated with Gardner syndrome, was found in only one case [15]. An infrequent change in the jaw were supernumerary teeth, which are also mentioned in literature as Gardner Syndrome pathognomonic [4, 14, 16–20]. Only in two cases were root abnormalities found. One of the patients had taurodontism and another root resorption. Both patients were male and were of similar age. We can therefore assume that root changes are not a common disorder in GS [6, 14].

CONCLUSION

The practically one hundred percent chance of colon cancer in patients with Gardner syndrome should prompt dentists to respond to the described disorders. Fast reaction and referring to a general practitioner will advance the treatment. Unfortunately, Gardner syndrome can quite often be overlooked by dentists or general doctors. This study can be helpful to diagnose GS. Dental treatment of patients with GS sometimes can be a challenge for the dentist, and tooth extraction has been reported to be likely difficult.

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