Received: 2 March 2018 | Revised: 29 October 2018 | Accepted: 30 October 2018

DOI: 10.1111/scd.12339

CASE HISTORY REPORT

WILEY

Gardner syndrome with maxillofacial manifestation: A case report

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Abstract

Gardner syndrome is a hereditary disease in which patients develop gastrointestinal polyps, osteomas, desmoid tumors, epidermoid cysts, fibromas, lipomas, and retinal lesions. Dental abnormalities such as supernumerary or impacted teeth, odontomas and dentigerous cysts are also reported. The most serious concern in this syndrome is the extremely high risk of gastrointestinal polyps undergoing malignant transformation. Since the maxillofacial findings usually precede gastrointestinal polyps, the dentist plays a crucial role in the diagnosis of Gardner syndrome, and panoramic radiography is an important tool in the diagnosis of the disease. We report here a case of Gardner syndrome in a patient showing mandibular osteomas and impacted teeth. Also, cases of Gardner syndrome with maxillofacial manifestations reported in the literature were reviewed and compared with ours. According to the findings, osteomas are important manifestations of this syndrome, and regardless of the absence of family history of intestinal polyposis, their occurrence should prompt diagnostic evaluation for this disease.

KEYWORDS

gardner syndrome, intestinal polyposis, osteoma

1 | INTRODUCTION

Gardner syndrome is an autosomal dominant inherited disorder with an incidence of 1:8300-16 000 births, characterized by bone malformation and the development of soft tissue tumors. It is a variant of familial adenomatous polyposis that may involve gastrointestinal polyps, osteomas, desmoid tumors, epidermoid cysts, fibromas, lipomas and retinal lesions.[1–4] Several dentomaxillofacial disorders such as supernumerary or impacted teeth, odontomas and dentigerous cysts have been described in a substantial number of Gardner syndrome patients.[5–8]

Diagnosis of Gardner syndrome is a challenging task due to the diversity of clinical manifestations. Some patients may present with few anomalies, whereas others have all the hallmarks of the disease.[9] It is important to recall that the onset of osteomas in the facial bones and skull precedes gastrointestinal polyposis, which in most cases develops during the second and third decades of life.[10,11] We report here a case of Gardner syndrome with maxillofacial manifestation, where the patient had been followed-up for 16 years.

2 | CASE REPORT

A 14-year-old male patient was referred for evaluation of 1-year painless bilateral facial swelling. Medical history was noncontributory for the diagnosis, and extraoral examination showed, through palpation, bilateral hard nodules in the posterior region of the mandible. No facial asymmetry

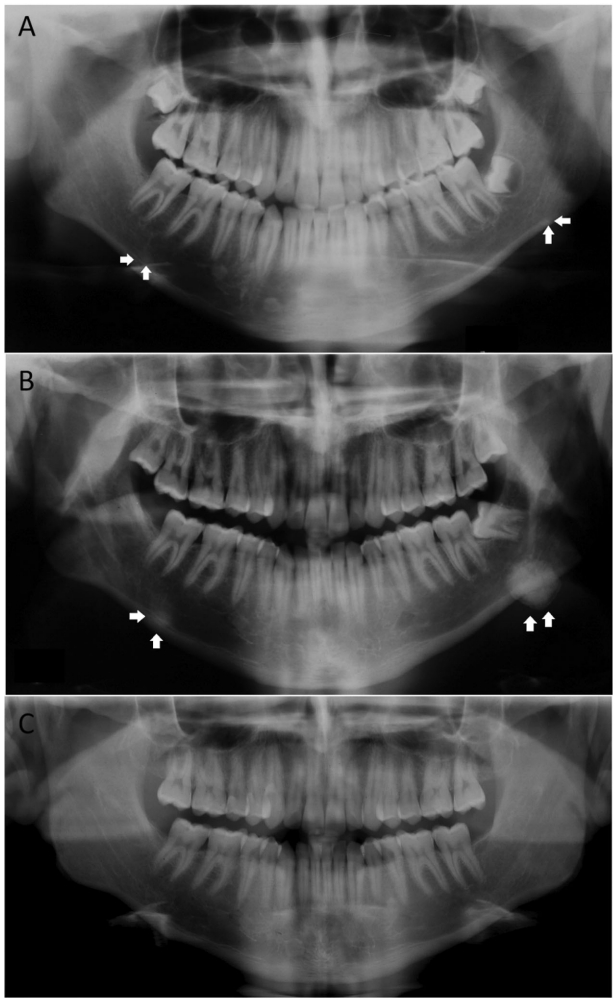

FIGURE 1 Panoramic radiograph shows slight radiopacities in the left posterior region of the base of the mandible and in the right mandibular body (A). Enlargement of both lesions at 3-year follow-up (B) and radiographic appearance at 16-year follow-up (C). Slight radiopacities corresponding to osteosclerosis can also be seen in the anterior region (canine, right) and premolar region (right) of the mandible, which showed no change during follow-up (A, B, C)

was detected, and intraoral examination did not reveal any other alteration. A panoramic radiograph revealed 2 slight radiopacities, one in the posterior region of the left base of the mandible and the other one in the right mandibular body (Figure 1A).

Clinical and radiographic features of the lesions were compatible with osteoma, and a follow-up was scheduled at first, since they were small and painless, with no functional or aesthetic compromise. Nevertheless, substantial enlargement occurred during the follow-up (Figure 1B), so surgical excision was performed. The panoramic radiograph also showed an impacted left mandibular third molar and partially erupted upper third molars (Figure 1B), which were extracted. Histopathological examination revealed trabecular bone with marrow spaces and osteoblasts in the lesion excised from the left side of the mandible, whereas compact bone was found in the right side lesion, which had minimal marrow spaces and occasional Haversian canals. These findings confirmed the diagnosis of osteoma for both lesions (Figure 2). The patient had no family history of adenomatous polyposis or other major disorders, but in view of the occurrence of multiple peripheral osteomas, he was advised to see a gastroenterologist to rule out intestinal polyps. Gastrointestinal evaluation and colonoscopy were scheduled late because of the waiting list of the public health system, and when the examination was finally performed, intestinal polyps were diagnosed. Histopathological examination of the surgical specimens revealed tubular adenomas with low grade dysplasia. Ophthalmic examination of the patient was normal, without any sign of hypertrophy of the retinal pigment epithelium. A diagnosis of Gardner syndrome was then established and a systematic monitoring of the patient was scheduled including panoramic radiography and colonoscopy with biopsy every year. At 15-year follow-up, due to a significant increase in the number of intestinal polyps, more than one hundred (Figure 3), a total prophylactic colectomy was performed. Afterwards, a gastroesophageal endoscopy showed polyposis with histopathological diagnosis of adenoma with low grade dysplasia. The patient has been clinically and radiographically evaluated at least once a year for 16 years, showing no signs of recurrence of the jaw lesions in sequential X-rays (Figure 1C). Table 1 presents a summary of the patient's follow-up.

3 | DISCUSSION

Gardner syndrome is characterized by multiple lesions involving the skeleton, skin, colon, and retina.[12] Its most serious involvement is the malignant transformation of intestinal polyps. The diagnostic criterion is based on the association of several features, mainly multiple intestinal polyps, osteomas, fibromas, and epidermal cysts.[13] The diagnosis is sometimes an incidental finding, since osteomas and dental abnormalities, which precede intestinal polyps, can be asymptomatic.[5,7] Table 2 presents the literature reports on Gardner syndrome with oral and maxillofacial signs. In the case we presented here, sufficient criteria for the diagnosis of the syndrome were met, since the patient developed osteomas, impacted teeth and intestinal polyps.

Gardner syndrome is linked to a mutation of the *adenomatous polyposis coli* (APC) gene located on chromosome 5 in the q21-22 region.[25] Mutations may result in various clinical phenotypes depending on where they occur along APC. The final gene product length determines the severity of gastrointestinal tract disease and the occurrence of retinal lesions or desmoid tumors.[26] Osteomas occur in patients within the mutation spectrum spanning codon 767 to codon 1513, whereas patients with mutations upstream or

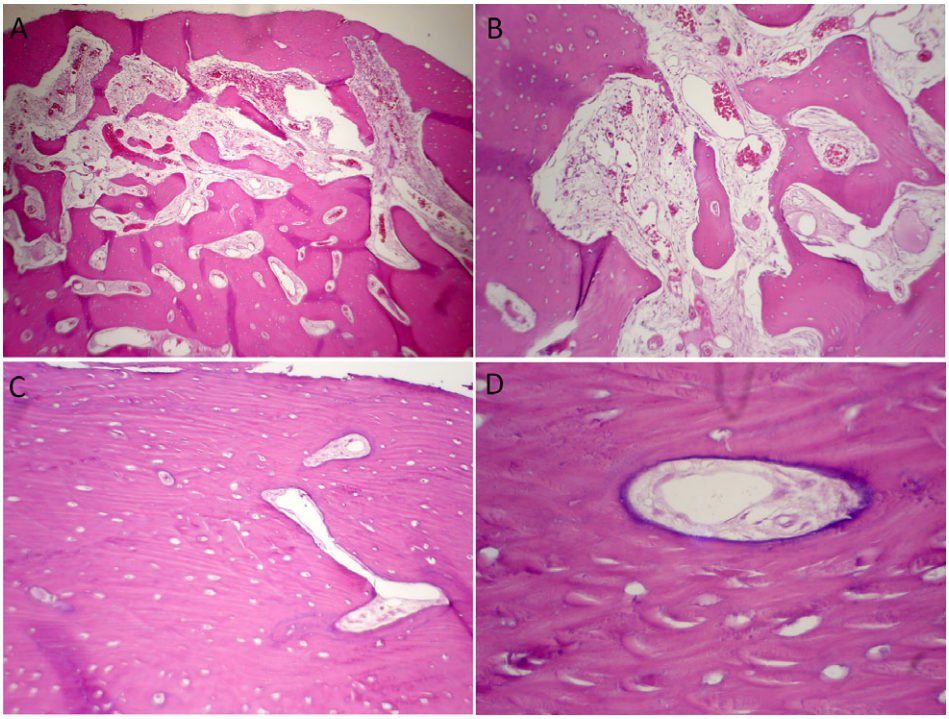

FIGURE 2 Histopathological appearance of the lesions with hematoxylin and eosin staining at 100× (A), 200× (B and C), and 400× (D). (A), (B) Lesion excised from the left side of the mandible, composed of medullary bone with peripheral trabecular bone and scattered fibrovascular connective tissue, filling the numerous intertrabecular spaces. (C), (D) The lesion excised from the right side of the mandible, showing compact bone. Both histopathological examinations were compatible with osteoma

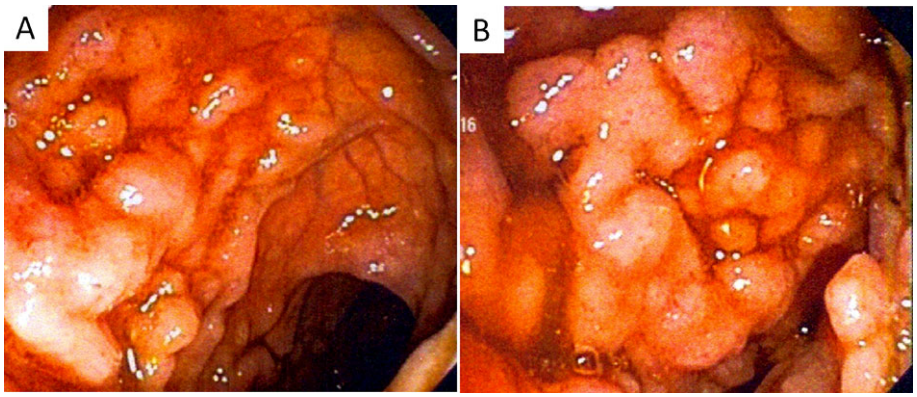

FIGURE 3 Colonoscopy revealed multiple intestinal polyps (A and B)

downstream of this region do not manifest them.[27] Asymptomatic osteomas of the jaws can be conservatively approached with clinical and radiographic follow-up. Surgical excision is an option for osteoma when it interferes with normal function or causes severe deformation. However, an individualized approach is recommended, considering the size and location of the lesion. In cases where a surgical approach is demanded, a well-defined treatment plan with minimum damage to adjacent structures is necessary to minimize sequelae.[28]

Considering the age of our patient and the absence of family history of intestinal polyposis, he initially underwent clinical follow-up of the nodules in the jaw. Nevertheless, with the enlargement of the lesions and histopathological confirmation of osteomas, the patient was referred for a gastrointestinal evaluation. One could point out that this evaluation and consequent Gardner syndrome diagnosis could have happened earlier in this case. However, even though the first colonoscopy was performed some years after the first clinical examination, it still occurred at a young age and before any malignant transformation of the polyps, allowing the disease to be monitored with further prophylactic interventions. Accordingly, patients who are diagnosed early by means of extraintestinal manifestations benefit from such prophylactic procedures.[27] The data

TABLE 1 Patient's clinical history

Date	Patient's events	Dentomaxillofacial approach	Oral and maxillofacial findings
2001-2005	Bilateral mandible swelling	Clinical-radiographic follow-up every 6 months	Radiopacity on right side remained stable at 0.5 cm in diameter Radiopacity on the left side increased from 0.3 cm to 2.0 cm Normal laboratory tests*
2005	Bilateral mandible swelling	Osteomas and third molars removed	Histopathological diagnosis: osteomas
2005	Immediate postoperative evaluation	Referral for gastrointestinal evaluation	No clinical/radiographic changes
2006	No events	3-month postoperative follow-up	Panoramic X-ray: normal bone in the operated area
2006-2009	No events	Follow-up every 6 months	No clinical or radiographic changes
2009	Gastrointestinal evaluation		
2010 (Dec)	Colonoscopy: intestinal polyposis; tubular adenoma with low grade dysplasia		
2012 (Jan)	Colonoscopy: intestinal polyps; tubular adenoma with low grade dysplasia		
2013	Patient without gastroenterological medical assistance in public health system due to bureaucratic problems	Follow-up every 12 months with panoramic X-ray	No clinical/radiographic changes
2014 (Dec)	Colonoscopy shows intestinal polyps with diagnosis of tubular adenoma with low grade dysplasia		
2015	Colonoscopy shows intestinal polyps with diagnosis of tubular adenoma with low grade dysplasia		
2016 (Jan)	Colonoscopy shows more than 100 intestinal polyps		
2017	Total colectomy		
2018	Gastroesophageal endoscopy: polyposis; adenoma with low grade dysplasia		

*Complete blood count; erythrocyte sedimentation rate; fasting glucose; serum calcium, phosphate, and alkaline phosphatase.

in Table 2 show that most case reports of Gardner syndrome with osteomas in the maxillofacial complex had a family history of the disease, which probably helped in the diagnosis process. It is also noted that for these patients the diagnosis in several cases occurred very early (minimum age = 12 years old), while for the patients without family history, the earliest age at the time of diagnosis was 25 years old.

Ideal management of Gardner syndrome cases would require genetic counseling.[29] Our patient did not have access to such evaluation, and we agree that this is a weakness in our report. Meanwhile, this case reinforces the possibility of this syndrome occurring at a very young age regardless of no family history of intestinal polyposis, and manifesting early as innocent osteomas and impacted teeth.

Lack of knowledge of Gardner syndrome can delay its diagnosis[21] compromising the patient's management. About 80% of patients manifest early signs of the disease in the maxillofacial complex.[6,8] A harmless feature such as osteomas in the jaws or supernumerary and impacted teeth detected in a routine panoramic radiograph may represent the first signs.[5,7] Therefore, the dentist plays a crucial role in the diagnosis. This professional must be aware of that and, in case of suspicion of the syndrome or family history of intestinal polyposis, the patient must be referred for appropriate gastrointestinal evaluation.[5,7,27]

TABLE 2 Literature reports on Gardner syndrome with osteomas and other oral and maxillofacial manifestations (in the last 10 years)

Reference	Sex/age (years)	Previous medical history	Family history	Site of osteomas	Other alterations	Management of osteomas and dental manifestations	Genetic counseling
Vaynsthein et al, 2008[14]	F/75	Not reported	Yes	Mandible and other bones of the face	Lipomas	No surgical excision of osteomas reported	No
Kamel et al, 2009[15]	F/24	Gardner syndrome	Yes	Frontal bone, mandible, maxilla, and ethmoid sinus	Odontomas, supernumerary, impacted teeth	Surgical removal of osteomas of the mandible	No
	F/23	Gardner syndrome	Yes	Frontal bone, mandible, maxilla, ethmoid, and maxillary sinus	Odontomas, impacted and missing teeth	Surgical removal of osteomas of the mandible and of impacted teeth	No
	F/22	Gardner syndrome	Yes	Frontal bone, mandible, maxilla, ethmoid sinus, frontal, and maxillary sinus	Odontomas, supernumerary, impacted teeth, and missing permanent teeth	No surgical excision of osteomas	No
	F/21	Gardner syndrome	Yes	Frontal bone, mandible, maxilla, ethmoid, and maxillary sinus	Odontomas, impacted teeth	No surgical excision of osteomas, removal of impacted teeth	No
Lee et al, 2009[16]	F/55	Not reported	Yes	Mandible, maxilla, ethmoidal sinus, and orbit	Impacted tooth, complex odontomas, desmoid tumor (abdomen)	No surgical excision of osteomas	No
De Oliveira Ribas et al, 2009[17]	M/25	Removal of sebaceous cysts	Yes	Mandible	Not reported	No surgical excision of osteomas	No
	F/12	Not reported	Yes	Maxilla, mandible, and left temporo-mandibular joint	Impacted teeth	Patient was no longer followed up	No
Silva et al, 2009[13]	F/25	Unremarkable	No	Palate, mandible, frontal, ethmoidal, and right maxillary sinuses	Compound odontomas, cementomas, unerupted tooth, epidermoid cysts	Surgical excision of osteoma, odontoma, and epidermoid cysts	No
Boffano et al, 2010[5]	F/25	Gardner syndrome	No	Maxilla, mandible, frontal, temporal, and zygomatic bone bilaterally	Impacted teeth, odontomas	Surgical excision of impacted teeth and osteomas	No
Brucoli et al, 2011[18]	M/25	Gardner syndrome, polypec-tomies	Yes	Mandible and maxilla	Missing a large number of teeth	Surgical excision of mandibular lesions	No
	M/52	Gardner syndrome, total colectomy	Yes	Mandible, frontal bone, and orbit	Not reported	Surgical excision of mandibular lesions	No
Fichter et al, 2011[19]	M/19	Not reported	Yes	Mandible	Not reported	Surgical excision of osteoma	No

(Continues)

TABLE 2 (Continued)

Reference	Sex/age (years)	Previous medical history	Family history	Site of osteomas	Other alterations	Management of osteomas and dental manifestations	Genetic counseling
Cristofaro et al, 2013[2]	M/46	Excision of osteomas, total colectomy, ileostomy	Yes	Mandible	Not reported	Surgical removal of multiple osteomas	Yes
	M/20	Excision of osteomas	Yes	Mandible and frontal bone	Not reported	Surgical removal of osteomas	Yes
Seehra et al, 2016[11]	F/12	Unremarkable	Yes	Mandible and maxilla	Impacted teeth, odontomas, osteomas	No treatment for dental conditions	Yes
Verma et al, 2016[20]	M/52	Abdominal cramps	No	Palate, maxilla, and mandible	Impacted teeth	Surgical recontouring of osteomas	No
Guignard et al, 2016[21]	M/23	Fibroma in parotid	Yes	Skull	Multiple polyps, desmoid tumors	Parotidectomy	Yes
Bouaoud et al, 2017[22]	M/13	Unremarkable	Yes	Mandible	Not reported	Surgical excision of mandibular lesions	No
	M/16	Unremarkable	Yes	Mandible	Not reported	Surgical excision of mandibular lesions	No
Adisen et al, 2018[23]	M/26	Removal of desmoid tumor in chest	No	Mandible and maxilla	Soft tissue tumor in shoulder	No surgical excision of osteomas	No
Vásquez Elera et al, 2018[24]	M/40	Not reported	No	Mandible	Not reported	No surgical excision of osteomas	No

F = female; M = male.

ACKNOWLEDGMENT

We thank Dr. A. Leyva (USA) for English editing of the manuscript.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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How to cite this article: Baldino ME, Koth VS, Silva DN, Figueiredo MA, Salum FG, Cherubini K. Gardner syndrome with maxillofacial manifestation: A case report. *Spec Care Dentist*. 2019;39:65–71. https://doi.org/10.1111/scd.12339