Oral manifestations of Gardner’s syndrome in young patients: report of three cases

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ABSTRACT. Background In young patients, multiple osteomas in the jaw and sebaceous cysts are signs which usually precede the diagnosis of Gardner’s syndrome. It is the association of multiple colonic polyps (familial adenomatosis polyposis coli) and extracolonic findings. By the fourth decade of life the colonic polyps undergo malignant transformation. Case reports The oral manifestations are described in three young patients diagnosed with Gardner’s syndrome that emphasises the importance of the role of the paediatric dentist in the early detection of multiple jaw osteomas and other dental abnormalities, which may lead to further investigation and treatment.

KEYWORDS: Gardner’s syndrome, Adenomatous polyposis of the colon, Familial adenomatosis coli, Osteomas.

Introduction

Gardner’s syndrome (GS) is characterised by multiple colonic polyps (familial adenomatosis polyposis coli) and by several extracolonic findings that often precede diagnosis. The extracolonic findings are: skeletal abnormalities (osteomas in the skull and mandible), dental abnormalities, skin tumors (fibrous tumors and sebaceous cysts), polyps of the stomach and small bowel, and characteristic retinal pigmentation [Lew et al., 1999]. The condition’s inheritance pattern is autosomal dominant with near 100% penetrance, but variable expression [Ahnen, 1990]. Approximately one third of cases may occur spontaneously and appear to represent new gene mutations [Neville et al., 2002]. The gene responsible has been mapped to chromosome 5 [Bodmer et al., 1987]. The reported incidence varies from 1:8,300 to 1:16,000 live births [Neville et al., 2002] and the mean age at the time of diagnosis of the polyposis is approximately 25 years [Bülow, 1986].

The colonic manifestation is the presence of numerous colorectal adenomatous polyps, which, if untreated, will transform into adenocarcinomas [Neville et al., 2002]. These polyps may appear before puberty [Antoniades et al., 1987]. By age 30, about 50% of patients with GS develop colorectal carcinoma and the frequency of malignant change approaches 100% in older patients [Neville et al., 2002]. Because of the tendency towards rapid malignant transformation of polyps, surgery of the lower intestine is performed to prevent transformation of any adenomatous polyps [Antoniades et al., 1987]. However, surgical intervention and connective tissue damage can induce desmoid formation in these patients, and for this reason some authors advocate trying to slow the progression of the polyps with medical treatment (for example, sulindac, tamoxifen) [Mohos et al., 2001]. For the sparse type of familial adenomatous polyposis, treatment with sulindac has been suggested in order to postpone prophylactic colectomy [Okai et al., 2001]. In any case, the long term prognosis of patients with GS depends on the rate of degeneration of these colonic polyps [Ruhin et al., 1998].

Extracolonic polyps may be found anywhere in the upper gastrointestinal tract. The most common sites are the duodenum, the pancreatic ampulla and the stomach [Jagelman et al., 1988]. Desmoid tumors are non-malignant, invasive and recurrent lesions that occur in approximately 10% of affected patients and are three times more common in women [Neville et al., 2002]. Pigmented lesions of the ocular fundus are evident in nearly 90% of these patients [Neville et al., 2002]. Ophthalmic fundoscopy is very important: patients with more than three congenital hypertrophies of the retinal pigment epithelium (CHRPE) in one eye or bilateral CHRPE in patients with a positive family history require further gastroenterological evaluation.
[Meyer et al., 2002]. In addition, an increased prevalence of thyroid carcinoma is also noted, with females demonstrating a 100-fold increase [Neville et al., 2002].

Up to 90% of the patients with GS demonstrate skeletal abnormalities, the most common of which are osteomas [Neville et al., 2002]. In most cases, the osteomas appear around puberty and precede the appearance of intestinal polyposis [Antoniades et al., 1987; Koppany et al., 2002]. Osteomas tend to grow slowly and become dormant once their size stabilises; there are no reports of osteomas undergoing malignant transformation [Sayan et al., 2002]. However, actively growing osseous tumors of the mandible have been reported [Antoniades et al., 1987; Takeuchi et al., 1993; Lew et al., 1999]. They vary from slight thickening to large masses, and may affect all parts of the skeleton; although the most frequent sites are the outer cortex of the skull, maxillary sinuses and the mandible. A particularly diagnostic site is the angle of the mandible [Antoniades et al., 1987; Lew et al., 1999; Payne et al., 2002], although these tumors have also been described in the condyle region [Lew et al., 1999].

Dental abnormalities include multiple unerupted and supernumerary teeth, odontomas, dentigerous cysts and hypercementosis [Arendt et al., 1989; Parks et al., 2001; Neville et al., 2002]. Oral examination may show palpably bony swellings or exostoses on mandibular angles and tenderness, in some cases limiting mouth opening [Ruhin et al., 1998; Lew et al., 1999]. Dental orthopantomography (OPG) may reveal well-defined opacities around the periphery of the mandible (exostoses) and multiple radiopacities throughout the mandible and the maxilla (enostoses) [Antoniades et al., 1987; Payne et al., 2002]. The enostoses are usually found in the premolar-molar region of both jaws and the number and size increase slowly with age. In some cases enlarged enostoses may cause resorption of the roots of adjacent teeth [Wolf et al., 1986]. Computer tomography (CT) scans may show the involvement of both bone and cemental proliferations [Yuasa et al., 1993]. The finding of more than three osteomas in the jaw by means of dental panoramic tomography is highly suggestive of GS [Ida et al., 1981]. Some cases require the resection of the osteomas, usually performed under general anaesthesia (GA), although removal does not guarantee freedom from recurrent disease [Lew et al., 1999].

**Case reports**

**Case 1**

A 10-year-old boy consulted our service with a chief complaint of a hard bilateral swelling on the angle of the mandible, of long-term evolution, which had become more noticeable in recent weeks. There was no family history of the condition.

Examination confirmed the presence of bilateral palpable bony irregularities on both mandibular angles, although the one on the right side was significantly larger. The texture of the overlying skin was normal. Moreover, the patient presented exostoses on the right maxilla, the parietal and occipital regions, and a soft tumour at the level of the L5, present since birth.

Oral mucosa was normal. The dental OPG showed multiple mandibular exostoses and enostoses. Moreover, the OPG revealed an unerupted mandibular right first premolar (44) and persistence of the mandibular right first primary molar (84) (Fig. 1a). The CT scan of the face and jaws showed many mature

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**FIG. 1 - A. OPG shows multiple osteomas on the mandibular angles and unerupted lower right first bicuspid (44) with persistence of lower right first primary molar (84). B. CT scan after first intervention on the right side shows multiple mandibular osteomas, specially on the left horizontal ramus.**
osteomas on the right and left angles, pterigoid plates and zygomatic arches.

_Treatment._ As these findings suggested a diagnosis of GS, the patient underwent a fibrocolonoscopy. No malignant transformations were found. The ocular fundus was normal.

_Follow-up._ One year later the growth of the right-side tumour required the resection of the osteomas under GA. Histologic examination revealed sclerotic bone tissue. During the following three years, the osteomas on the left side grew considerably (Fig. 1b), and so the tumors on this side were resected. At this stage, the tumours previously operated on the right-side presented minimal growth.

The patient is currently being followed-up by specialists in gastroenterology, surgery and ophthalmology.

**Case 2**

A 9-year-old girl presented at the Hospital Dental Service with a chief complaint of delayed eruption of her permanent maxillary right central incisor (11). She had previously been diagnosed with GS and her family’s medical history was significant in that her maternal grandfather had presented multiple desmoid cysts and had died of colon cancer. Her mother had several sebaceous cysts and mandibular exostoses, but no history of digestive pathology.

At the age of six months, the patient had presented a desmoid tumour on her back and small bony tumors on her skull. At age two years, she underwent resection of the paravertebral desmoid tumor but it recurred within two years. The biopsy revealed a desmoid tumor (infantile fibromatosis). At this stage, she presented multiple exostoses on her frontal and parietal bones. It was not until age 10 years that the fibrocolonoscopy revealed the presence of four colonic polyps; the patient was prescribed palliative treatment with sulindac. The ocular fundus was normal and genetic examination identified the APC gene on 5q21-22.

The dental clinical examination at age 9 revealed the absence of the maxillary right permanent central incisor (11). The dental OPG showed a supernumerary tooth impeding the eruption of the maxillary right central incisor (Fig. 2a).

_Treatment._ The supernumerary tooth was extracted under GA. The panoramic radiograph after tooth extraction showed several well-defined opacities throughout the mandible (Fig. 2b).

_Follow-up._ Six months later, after orthodontic treatment, the permanent incisor still showed no eruptive movement, so the decision was taken to extract the permanent tooth and to close the space with orthodontics.

**Case 3**

A 17-year-old girl was referred by the Hospital’s Maxillofacial Surgery Service for multiple dental anomalies. Her family history was uneventful. Her medical history described the presence of two tumours in her abdominal wall, which were resected under GA at age 2 and at age 6 and diagnosed as non-specific myofibromatosis. Moreover, at age 15 a desmoid cyst in her back was observed, which was resected. Histologic examination revealed an epidermal cyst.

Dental examination confirmed the presence of extensive caries in eight permanent molars and several premolars. The presence of primary teeth (52 and 63) was noted, with the respective absence of the maxillary right permanent lateral incisor (12) and left canine (23). The OPG confirmed the inclusion of 12 and 23 in an ectopic position, as well as the presence of two odontomas, one at the apical level of 52 impeding eruption of 12, and the other between incisors 21 and 22. A supernumerary tooth between the apical regions of 22 and 63 was also observed. The osseous mandibular base showed a marked antegonial notch on the right side. The differences in bone

![Fig. 2 - A. Dental OPG shows a supernumerary tooth impeding the eruption of the upper right central incisor (11). B. The OPG after extraction of the supernumerary tooth shows several well-defined opacities throughout the mandible.](image-url)
density, especially in the mandible, and the enostoses between the roots of 35 and 36 were significant findings (Fig. 3a).

Treatment. As these results were suggestive of GS, a colonoscopy was recommended, but the patient refused. Ophthalmic funduscopy was normal. The decayed molars were extracted under GA together with the ectopic teeth 12 and 23 and the apical odontoma at 62. Multiple amalgam restorations were performed (Fig. 3b).

Table 1 shows the general and oral findings of the three clinical cases.

**Discussion**

The diagnosis of GS in the adult patient is usually based on the detection of colonic polyposis or other extracolonic findings. Asymptomatic descendants at risk require a systematic rectosigmoidoscopy as a screening examination [Wolf et al., 1986]. GS has high potential for malignancy [Buch et al., 2001] and is associated with high mortality rates in undiagnosed cases [Antoniades et al., 1987]; accordingly, an early diagnosis is vital. Early manifestations, such as desmoid tumours, bone and dental anomalies, are key signs which can allow prompt diagnosis. Early detection, while essential, can be difficult because of attenuated phenotypes or spontaneous mutations [Wehrli et al., 2001]. We believe that two of our clinical cases (Case 1 and 3) are probably spontaneous mutations of the disease, as none of the parents of either patient had a family history of adenomatosis polyposis coli.

The three young patients described here, presented oral manifestations compatible with GS, even though only one case (Case 2) showed the complete clinical picture of the syndrome, that is, a history of colonic polyposis. Nevertheless, we believe that it is only a matter of time before the other two patients show the complete manifestations of the syndrome.

**Table 1** - General and oral findings in the three cases of Gardner’s syndrome.

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M = Male; F = Female; + = Positive; - = Negative; * = Undetermined
cannot be ruled out, and so the patients must be examined periodically [Herrmann et al., 2003].

If clinical palpation of the jaws suggests the presence of multiple osteomas, a dental panoramic tomography is a useful initial investigation [Payne et al., 2002]. In young patients with no palpable exostoses, an orthopantomogram may reveal multiple radiopacities (exostoses) throughout the mandible and the maxilla [Antoniades et al., 1987; Payne et al., 2002]. Computer tomography is also an important tool for the diagnosis of this disease, especially as it is able to show wavy cortical thickening on the buccal side of the mandible (something that panoramic radiography is unable to do) [Yuasa et al., 1993].

Bone abnormalities are seen in all three patients, although one presented more evident osteomas and showed a more aggressive pattern which required surgical treatment (Case 1). In the others, the mandibular exostoses were a casual radiographic finding (Case 2 and 3). Other dental abnormalities observed were odontomas, unerupted and supernumerary teeth (Table 1).

We believe that the eruptive alterations of permanent teeth observed in all three cases may be due to osseous abnormalities and not to alterations of the dental follicle; this would explain the failure of orthodontic traction of the unerupted tooth in Case 2. In any case, dental care of patients should be started as early as possible, because dental and jaw changes may later cause serious dental problems [Wolf et al., 1986].

### Conclusion

Patients with GS present a wide variety of manifestations, and must be diagnosed and treated as early as possible.

These patients will require multidisciplinary care for the rest of their lives. Because oral findings usually precede the gastrointestinal manifestations, the role of the pediatric dentist is vital in the detection of the signs stigmas as he or she is likely to be the first healthcare professional to diagnose the condition [Wolf et al., 1986; Antoniades et al., 1987; Payne et al., 2002].

### References


