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The head and neck features of Gardner's Syndrome: A case report and review of the literature

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ABSTRACT

Background

Gardner's Syndrome represents an autosomal dominant variant of Familial Adenomatous Polyposis in which affected individuals have a 100% risk of developing colorectal carcinoma. The extra-intestinal manifestations in the head and neck region allow for the early recognition and diagnosis of this rare syndrome. The defining triad of features includes intestinal polyposis, dento-osseous anomalies and soft tissue lesions.

Methods

A 20-year-old female patient presented with a main complaint of swelling involving the left side of her nose, at which time a panoramic radiograph was obtained.

Results

Radiographic findings showed multiple osteomas, odontomas, missing teeth as well as unerupted and impacted teeth, the features of which are highly suggestive of Gardner's Syndrome.

Conclusion

Early recognition of the extra-intestinal features of Gardner's Syndrome warrants patient referral for further investigation including colonoscopy and genetic testing.

Keywords

Gardner's Syndrome, osteomas, intestinal polyposis, odontomas, supernumerary teeth, epidermoid cysts

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Conflict of interest

The authors declare they have no conflict of interest.

INTRODUCTION

Gardner's Syndrome (GS) is a rare condition initially defined as an autosomal dominant (AD) hereditary form of colonic polyposis which occurs in association with osteomas and multiple cutaneous and soft tissue tumours.[1-3] Patients with undiagnosed GS are at almost 100% risk of developing colorectal carcinoma in the third to fourth decades of their lives with a reported incidence of death occurring at 41 years of age.[1,4,5] A spectrum of extra-intestinal manifestations has been documented, all of which precede the intestinal polyposis and its malignant transformation.[1,3,6,7] The extra-intestinal manifestations, particularly those occurring in the head and neck region, should always be viewed with a high index of suspicion by the oral health care worker (OHCW). For this reason, OHCWs should have at least some basic knowledge regarding the dental and craniofacial features associated with GS.[8] Furthermore, any extra-oral or skin lesions of the head and neck region as well as the appearance of the oral mucosa should be thoroughly examined in order to document any related lesions or changes. Cutaneous findings associated with GS include epidermoid cysts, desmoid tumours and occasionally other benign skin neoplasms such as lipomas.[1,2] Some 50%-65% of patients with GS present with multiple asymptomatic epidermoid cysts predominantly involving the face, scalp and occasionally the extremities.[1,2] The extra-intestinal head and neck manifestations of GS may easily be recognised at dental consultation with plain film panoramic radiography. Dental anomalies linked to GS are found in 30%-75% of patients. These may include impacted and supernumerary teeth, as well as areas of idiopathic osteosclerosis. These signs are important clues for diagnosis and should not be overlooked.[8] The osteomas in GS are benign bone forming lesions composed of well differentiated mature bone tissue with a predominant laminar structure. Multiple osteomas are usually identified in GS patients with the mandible most often being involved. Skull and maxillary involvement are also frequent. Mandibular osteomas may appear solitary or as lobulated masses of bone. Solitary (central) osteomas are usually located at or near the apices of teeth, while lobulated osteomas tend to be cortical in nature and are frequently encountered in the mandibular angle area. Osteomas are relatively asymptomatic and slow growing, but may reach proportions which cause facial distortion, asymmetry and even result in chewing disorders and limitation of mouth opening. Large osteomas may even compromise adjacent structures to the extent that swallowing and breathing may be compromised. The craniofacial and dental features may thus be some of the most significant indications of the need for care to prevent malignant transformation of intestinal polyposis and may

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indeed be of life-saving importance.[2,9,10] The vigilant OHCW should thus be prompted to refer the patient for further gastrointestinal and genetic testing.[8,9,11,12] The pertinent dental findings may indeed serve as a form of colorectal cancer screening in this subset of patients.[8,13]

The following case report intends to highlight the essential role of the OHCW in identifying cutaneous, dental and osseous features which are suspicious for underlying GS. It further demonstrates that the craniofacial and dental manifestations of the syndrome can be detected as early as the second decade of life and may thus be pertinent in preventing the early mortality documented in undiagnosed patients with GS.

CASE REPORT

A 20-year-old female patient presented to the Department of Oral and Maxillofacial Surgery at the Sefako Makgatho Oral Health Centre with a main complaint of swelling on the left side of her nose which had been present for several years. The patient reported that the lesion was painful and had been swelling and receding for several years. The patient was in good health with no significant medical history and, to her knowledge, no other family members had reported or experienced a similar condition. Intra-oral examination revealed several missing teeth, a bulbous soft tissue protrusion emanating from the buccal mucosa in the second quadrant, and purulent discharge was present in the region of teeth 24 and 25. Extra-oral examination revealed a swelling above the left cheek. No abnormalities were detected on examination of the temporomandibular joints (TMJ). A panoramic radiograph obtained at this appointment showed features in keeping with GS. The radiological features are demonstrated in Figure 1.

Clinical findings were further explained to the patient highlighting the complexity of this case. To alleviate pain and purulent discharge in the second quadrant and after ensuring that informed consent was obtained from the patient, local anaesthesia (2% lignocaine, Xylotox) was administered and teeth 24 and 25 were surgically extracted. A small portion of bone was removed from within the sockets and submitted for histological evaluation. The patient was prescribed antibiotics (1000mg Augmentin, one tablet twice daily for 5/7 days), analgesics (1000mg Paracetamol and 400mg Ibuprofen, two tablets every 6 hours when necessary for pain for 7/7 days), and mouthrinse (0.2% chlorhexidine digluconate, rinse with 10ml twice daily for 5/7 days). The patient was seen one week later for follow-up, at which time wound healing was proceeding well.

The most striking features on examination of the panoramic radiograph are multiple osteomas located predominantly within the angle and ramus area of the left mandible. Similar smaller lesions are present within the posterior right mandibular body distal to tooth 47. The osteomas located in the left mandibular angle and ramus area form well circumscribed radiopaque lesions of variable size. One of these is located at the angle of the mandible appearing to have formed peripherally as a periosteal lesion. A second osteoma is peculiarly located within soft tissue as an extra-osseous variant and is located within the space between the coronoid process and the condylar head. The remaining osteomas in this region are located within the ramus region, appearing to be extra-osseous in subtype.

Within the first quadrant there is an unerupted tooth 11, missing tooth 12, retained 53 with impaction of teeth 13, 14 and 15. The roots of tooth 16 are indistinct. Tooth 18 is impacted. Within the anterior maxilla in the region of tooth 11 is a circumscribed radiopaque lesion surrounded by a radiolucent halo, the features of which are in keeping with a complex odontome.

Within the second quadrant are impacted teeth 23, 24 and 25. Between the roots of the impacted 24 and 25 is an ill-defined lesion which appears to comprise multiple tooth-like radiopacities in keeping with a compound odontome. Tooth 28 is impacted because of a lack of space.

Within the third quadrant is an impacted and misshapen tooth 32 while both teeth 33 and 34 are impacted and

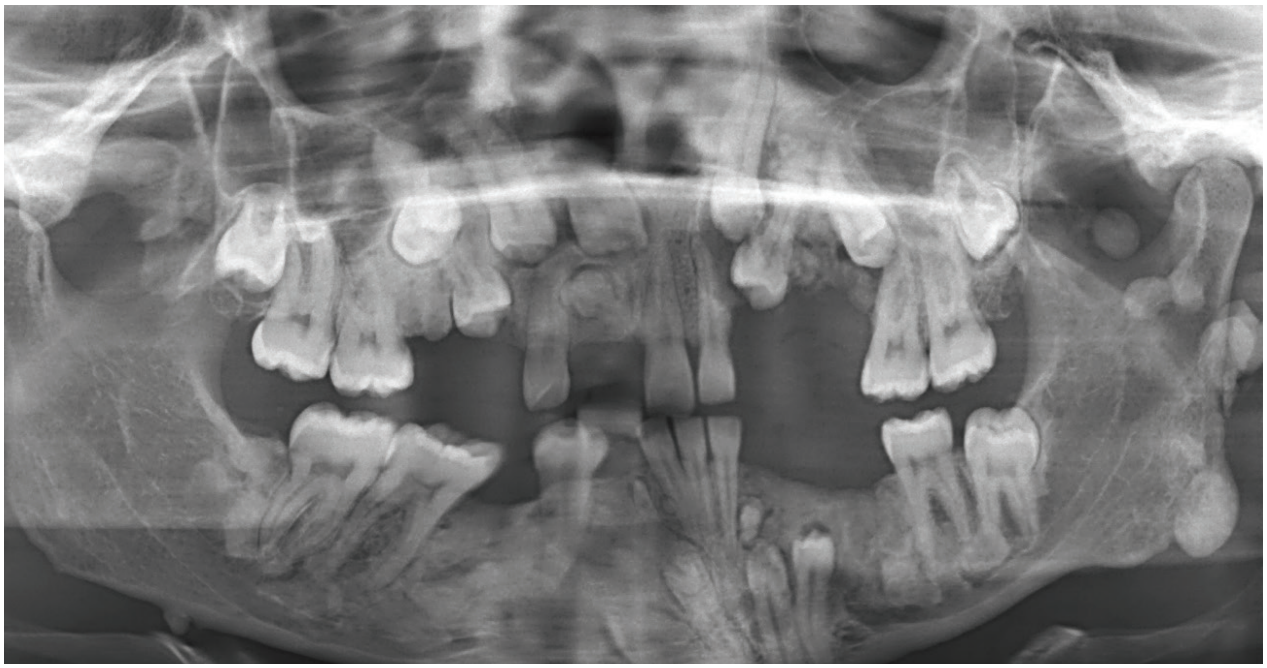

Figure 1: Panoramic radiograph showing features suggestive of Gardner's Syndrome.

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displaced inferiorly towards the lower border of the mandible. Tooth 35 is missing. An endosteal osteoma is located on the mesial aspect of the mesial root of tooth 36 while a similar lesion is present on the mesial aspect of tooth 37. Tooth 38 is missing.

Examination of the fourth quadrant shows an impacted tooth 43. Between the impacted 43 and the dilacerated root of tooth 44 is an indistinct mixed radiolucent/radiopaque lesion which may possibly represent an odontome which is located out of the plane of section. Tooth 45 and tooth 48 are both missing. A possible endosteal osteoma is located on the distal aspect of tooth 47 while an additional smaller periosteal osteoma is identified along the lower border of the right body of the mandible.

This panoramic radiograph shows the presence of more than 3 recognisable osteomas in addition to multiple dental anomalies including impacted and unerupted teeth, odontomas and missing teeth. These features are both highly suggestive and predictive of the diagnosis of Gardner's Syndrome. The age of the patient, considering the possible life-threatening complications of Gardner's Syndrome, is fortuitous as this may allow for timeous intervention if diagnostically confirmed. It is exigent that this patient be referred to a gastroenterologist as well as a geneticist for colonoscopy examination and genetic testing for APC gene mutations respectively. Furthermore, this patient will require extensive dental intervention for which prosthodontic, orthodontic and maxillofacial surgical assessment is required. While it appears that the osteomas are asymptomatic at present, surgical excision will be warranted if there is any facial asymmetry on growth or if examination shows any interference with mandibular function or dental occlusion.

DISCUSSION

Gardner's Syndrome (GS) is a clinical variant of Familial Adenomatous Polyposis (FAP) in which there is functional inactivation of the tumour suppressor gene Adenomatous Polyposis Coli (APC). The exact breakpoint at which the mutation occurs on chromosome 5q is unknown but varies from q13 to q31. More than1400 mutations have been identified. This is responsible for the wide array of clinical manifestations seen in GS.[2-4] The site on chromosome 5q2, however, determines that affected patients develop intestinal polyposis which have the potential to undergo malignant transformation.[4] GS is inherited in an autosomal dominant (AD) mode.[4] Truncating mutations of band 5q21-q22 results in the formation of a multidomain, multifunctional protein involved in Wnt signalling and microtubule function. There is no racial or gender predilection for GS.[4] Familial clustering is seen in most cases of GS; however, in up to one third of patients, GS occurs spontaneously due to de novo mutations.[3,13]

The traditional triad of features which defines Gardner's Syndrome includes intestinal polyposis, dento-osseous lesions and soft tissue lesions.[1,14] The extra-intestinal manifestations are generally noted earlier than the intestinal pathology which, although largely asymptomatic, would alert the most astute clinician to the possibility of underlying GS.[4] The most consistent feature in all patients is, of course, the presence of intestinal polyposis which affects the small and large intestines and occasionally the gastric mucosa. The polyposis is initially asymptomatic but develops within the second to early third decades. Polyps are present in most patients at around the time of puberty. Patients develop hundreds to thousands of benign adenomas – usually tubular, villous and tubulo-villous subtypes, which literally carpet the luminal aspect of the bowel. The polyps slowly enlarge in size and are known to increase in number with an increase in age.[3,13] Early clinical signs and symptoms attributed to the polyps may include anaemia, constipation, bloody diarrhoea, bowel obstruction, mucous discharge and abdominal pain.[4] Larger polyps may prolapse through the anus or have the potential to cause bowel obstruction by intussusception or ileus.[3] The polyps are initially smaller than 5mm representing benign adenomas which slowly begin to transform via dysplastic change in the classically described adenoma-carcinoma sequence. This illustrates the multistep carcinogenic process which is hastened in patients with pre-existing inflammatory bowel disease, a diet low in fibre and high in fat, in patients with a sedentary lifestyle, obesity and in those who smoke and consume alcohol. Malignant transformation is almost inevitable due to the sheer number of polyps inherently part of GS. Untreated GS has 100% risk of malignant transformation in which the average age of death of a patient with colorectal carcinoma is 41 years. This is more than 25 years earlier than the age recorded for death in patients with isolated colon cancer in the general population.[4,7]

The dento-osseous manifestations of GS include multiple osteomas which have a predilection for occurrence within the craniofacial bones, particularly within the mandible. They may also be identified within the maxilla, paranasal sinuses and less frequently within long bones.[11] Osteomas are benign bone forming lesions which slowly enlarge in size and remain asymptomatic. Surgical excision is only necessary for large lesions which cause facial asymmetry or unesthetic facial outgrowths or rarely if their location interferes with mandibular function or dental occlusion.[15] Osteomas present as circumscribed radiopaque masses. They tend to be quite numerous within the mandible and are easily diagnosed on plain film panoramic radiography as a coincidence at routine dental examination.[15] Osteomas are present in 90% of patients with GS with up to half of all patients presenting with three or more osteomas in the maxilla or mandible.[11,15] This alone is an indication of possible GS which should indicate that further investigation is required.[9]

There are a multitude of dental anomalies common to GS including supernumerary teeth, unerupted and impacted teeth, missing teeth, hypercementosis, hypodontia, compound odontomas and abnormal tooth morphology, many of which are present in this case. Within the adjacent jawbone there are often multiple areas of idiopathic osteosclerosis. It is interesting to note that the highest number of dental anomalies are usually identified in patients with multiple osteomas; however, the dental abnormalities may be identified in the absence of osseous involvement and do not occur secondary to bone lesions.[10]

The soft tissue manifestations of GS include cutaneous lesions and soft tissue neoplasms. The most common cutaneous lesions seen in association with GS are epidermoid cysts which are usually located on the skin of the scalp. These are present in up to 65% of patients with GS. These cysts are easily recognisable clinically and arise pre-pubertally and may also be seen on the skin of the face and

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extremities.[10] Unusual skin pigmentation may also be seen. Soft tissue neoplasms are generally of a benign nature and include lipomas, neurofibromas and leiomyomas. Desmoid tumours are rare subcutaneous lesions located within the abdominal and retroperitoneal regions. They are potentially difficult to manage due to their relentless recurrence.[2,10]

The relatively simplistic method of identifying possible patients with GS by recognising the head and neck manifestations of disease, should be entrenched in the dental education of all OHCWs, thus increasing their vigilance for any signs or symptoms to suggest its presence. This is critical to intervene and to refer for further investigation. Although more than three craniofacial osteomas are highly predictive of the presence of GS, the World Health Organisation has documented specific diagnostic criteria for its formal diagnosis. The three diagnostic criteria which the WHO has identified include 100 or more colorectal polyps; an APC germline mutation; and a family history of FAP and at least one epidermoid cyst, osteoma or desmoid tumour.[4]

Patients who present with suggestive features should be referred for genetic testing and colonoscopy. If the results are confirmatory, all family members should likewise be evaluated for Familial Adenomatous Polyposis.[7] Patients with GS may have to undergo a prophylactic colectomy if they are recognised as high risk. Furthermore, it is imperative that all cases be documented in order to raise awareness among health care personnel and for epidemiological purposes.[13]

Following extraction of the teeth 24 and 25 in this patient, the patient was fully informed of the underlying risk of possible GS and was therefore referred for colonoscopy and genetic testing. We have yet to receive any feedback with regard to the results of this referral.

CONCLUSION

The patient who presents with suspected GS should be subjected to comprehensive intra- and extra-oral examinations which may reveal any lesions seen in association with GS involving the skin or mucosa. An accurate medical history including a family history should be well documented. It is imperative that such patients be referred for specialist investigation and follow-up including colonoscopy, genetic testing and counselling.

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