Gardner’s Syndrome—The Importance of Early Diagnosis: A Case Report and Review of Literature

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ABSTRACT

Gardner's syndrome (familial polyposis coli) is a genetic condition characterized by colonic polyps that carry a 100% risk of malignancy if untreated. Early diagnosis, in which an astute and knowledgeable dentist can play an essential role, is therefore of paramount importance. The presence of osteomas and multiple unerupted teeth provides the dentist with a major pointer to the possible presence of this disease, which may be provisionally diagnosed on the detection of other obvious features, like the cutaneous lesions. This fact is clearly illustrated by the accompanying case report of Gardner's syndrome in a middle aged female patient who presented with the typical dental manifestations of the syndrome and timely detection of other manifestations halted the dreaded disease from further progression.

Keywords: Familial adenomatous polyposis (FAP), Epidermoid cyst, Desmoid tumor, Peripheral osteoma, Dental abnormalities, Colon carcinoma, Gardner's syndrome.

INTRODUCTION

In 1953, Gardner described a syndrome consisting of hereditary intestinal polyposis with osteomas and multiple cutaneous and subcutaneous lesions.1 This syndrome has since been modified by the addition of other features such as dental abnormalities, abdominal desmoids tumors and a number of malignant tumors. estimated to be between 1 in 12000 and 1 in 1400.2 The frequency of FAP-Gardner syndrome has been estimated to be between 1 in 12,000 and 1 in 1,400 live births.3 The inheritance pattern is autosomal dominant with complete penetrance. However, approximately 20% of cases represent spontaneous mutations, with no family history reported.5

We report a rare case of Gardner’s syndrome with spontaneous mutation diagnosed in Oral Medicine Department and demonstrating the full spectrum of dental, colonic and extracolonic manifestations.

CASE REPORT

A 33-year-old female patient reported to the Department of Oral Medicine and Radiology, Modern Dental College and Research Center, Indore, Central India with a chief complaint of a large swelling along the border of the lower jaw on the left side (Fig. 1). The patient was unable to recall precisely, when she first became aware of the swelling but pointed out that she had been aware of the slow but steady increase in the size of the swelling since the past 6 to 7 years. There was no history of pain and the patient was concerned about the large swelling for esthetic reasons. There was no history of trauma, discharge or bleeding from the affected area. Patient was comfortable in performing the routine jaw functions inspite of the large size of the swelling.

We report a rare case of Gardner’s syndrome with spontaneous mutation diagnosed in Oral Medicine Department and demonstrating the full spectrum of dental, colonic and extracolonic manifestations.
Extraoral examination revealed facial asymmetry due to a large bony hard swelling along the lower border of the mandible on the left side approximately 3 × 5 cm in diameter mimicking an osteoma. Bony outgrowths of similar nature on inspection and palpation but of variable sizes were present on the forehead region, in the right maxilla and anterior to the large swelling. Lymph nodes were nonpalpable.

Intraoral examination revealed multiple retained deciduous teeth (54, 55, 63, 73, 74, 75, 85), missing teeth (24, 25) and bony exostoses in all four quadrants of the jaws mainly in the premolar region (Figs 4A and B).

After careful history recording and clinical examination the clinical suspicion of Gardner’s syndrome was raised and patient was subjected to additional investigations like OPG, CT scan, Genetic testing, endoscopy, colonoscopy and barium meal to confirm the diagnosis. Laboratory investigations like CBC and blood biochemistry were normal.

OPG revealed multiple dense, homogenous radiopacities suggestive of compact osteomas present in the right sigmoid notch region and in the left coronoid process region. A single large osteoma having sharp borders was present attached to the left lower border of the mandible. The jaw bones also revealed a generalized diffuse radiodensity, a feature documented in the
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The panaromic radiograph also showed multiple impacted supernumerary teeth, unerupted permanent teeth, retained deciduous teeth and compound odontomes (Fig. 5). The CT scan of PNS revealed additional bony protruberances in the frontal, parietal and temporal vaults (Fig. 6). The paranasal sinuses were clear.

Genetic testing revealed a mutation in the adenomatous polyposis coli (APC) gene confirming the diagnosis of FAP.

On colonoscopy she was found to have numerous polyps carpeting the entire colon and rectum which was consistent with familial adenomatous polyposis (Figs 7A and B). Most of the polyps measured just about a centimeter in diameter. Histopathologic examination of the colonic polyps revealed adenomatous polyyp with mild dysplasia (Figs 8A and B). An upper endoscopy revealed normal findings.

A fundoscopic examination was performed showing the typical hypertrophy of the pigmented layer of the retina.

The patient is presently under the care of a colorectal surgeon and is listed for a restorative proctocolectomy with ileal pouch anal anastomosis with mucosectomy. This procedure is preferred because they attempt to eliminate all colon and rectal mucosa, thereby assuring the lowest risk of developing colorectal cancer.

DISCUSSION

In 1953, Gardner described a syndrome consisting of hereditary intestinal polyposis with osteomas and multiple cutaneous and subcutaneous lesions. At one time, Gardner syndrome was
thought to be a separate entity from familial adenomatous polyposis (FAP). However, it is now accepted that it represents one end of the spectrum of that disorder, and around 50% of those with FAP have extracolonic manifestations, although these are often subclinical. The frequency of FAP-Gardner syndrome has been estimated to be between 1 in 12,000 and 1 in 1,400 live births, affecting both genders equally, with a uniform worldwide distribution. The average age at diagnosis is 34.5 years to 43 years.

The inheritance pattern is autosomal dominant with complete penetrance. The FAP-Gardner syndrome gene has been localized to a small region on the long arm of chromosome 5(5q 21-22), referred to as the adenomatous polyposis coli locus. However, approximately 20% of cases represent spontaneous mutations, with no family history reported.

Of the two types of hereditary polyposis diseases: adenomatous – which includes familial adenomatous polyposis (FAP) and hamartomatous; Gardner’s syndrome is a variant of FAP affecting 10% of FAP patients. They have a 100% potential for malignant change, which usually occurs in the 20-40 years age group. The polypos commonly develop at around the time of puberty, and may occur in any part of the gastrointestinal tract, although the colorectal region is invariably affected.

One among the mesodermal lesions includes skeletal abnormalities, the most common of which are osteomas, an essential component of Gardner’s syndrome. These benign tumors are characterized by slow, continuous growth and most frequently in the mandible, the outer cortex of the skull and the paranasal sinuses. The angle of mandible is a particularly diagnostic site. The masses are sometimes of considerable size, and, nevertheless, may not give rise to a corresponding amount of swelling due to the fact that a part of the tumor is submerged in bone. They are almost always sessile and pedunculation is unusual. They may present either as an exostoses or enostoses. Histologically, these osteomas are of compact or ‘ivory’ type comprising dense compact bone with few marrow spaces and with only few osteons. The radiographic appearance of either type is a localized radiopaque lesion of homogenous density with a sharp border. Another type of lesion has been described with widespread radiopacity of the jaw bones in a patient with familial adenomatous coli. These bone tumors are known to occur at puberty and precede the presentation of the polyps.

Dental abnormalities are present in around 30% of patients with Gardner’s syndrome, and may include supernumerary teeth, compound odontomes, hypodontia and impacted or unerupted teeth. The highest incidence of dental abnormalities is found in patients with multiple osteomas. The incidence of supernumerary teeth is however not as high as seen in cleido-cranial dysplasia. The most common ectodermal abnormalities found are epidermoid cysts, frequently associated with lipomata, desmoid tumors, fibromas, leiomyomas, neurofibromas or pigmented skin. The multiple epidermoid cysts present in around 50-60% of patients are uncommon prior to puberty and occur primarily on the face, scalp and extremities. Their occurrence prior to puberty should alert the physician to evaluate the colon and the rectum for polyps. They have no malignant potential. Desmoid tumors may occur in the skin of anterior abdominal wall or intra-abdominally. Overall, the incidence of desmoid tumors in patients with FAP is 89%. They are usually slow growing deep fibromatoses that are histologically benign and have no metastatic potential. They are, however characterized by aggressive infiltration of adjacent tissue, and are prone to recurrence after surgical excision.

Other neoplasias strongly associated with Gardner’s syndrome include papillary carcinoma of the thyroid, which primarily affects female patients, tumors of the CNS such as glioma and medulloblastoma and periaipillary carcinoma of the duodenum. Many others including adrenal adenoma and adenocarcinoma, hepatocellular carcinoma, osteosarcoma, chondrosarcoma and osteochondroma have also been reported.

Asymptomatic pigmented ocular fundic lesions are present in more than 90% of patients with FAP or Gardner’s syndrome. It has been suggested that the presence of congenital hypertrophy of the retinal pigment epithelium, if demonstrated in relatives, is almost 100% predictive of FAP.

CONCLUSION

The cases of Gardner’s syndrome reported in the past describe only a few of the wide spectrum of manifestations of this rare disorder. To the best of our knowledge, this is the first case of Gardner’s syndrome with spontaneous mutation diagnosed in Oral Medicine Department and demonstrating the full spectrum of dental, colonic and extracolonic manifestations. Timely detection of these manifestations halted the dreaded disease from further progression.

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