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Síndrome de Gardner, uma variante da polipose adenomatosa familiar: um relato de caso

| Gardner's Syndrome, a variant of familial adenomatous polyposis: a case report

RESUMO | Introdução: *A síndrome de Gardner é uma doença rara, autossômica dominante, associada à mutação do gene Adenomatous polyposis coli (APC), caracterizada por polipose colônica com histopatologia compatível com adenoma, associada a tumores mesenquimais, como do tipo desmoide, osteomas e alterações dentárias. As manifestações extraintestinais podem ser os primeiros achados, sendo importante o conhecimento e divulgação do quadro clínico, permitindo diagnóstico precoce, manejo adequado e investigação familiar.* **Relato de caso:** *O objetivo deste relato de caso é descrever o caso clínico de polipose adenomatosa familiar, com variante compatível com Síndrome de Gardner, em paciente com manifestações extraintestinais com tumor desmoide, dentes supra numéricos e osteomas, em acompanhamento na Unidade do Sistema Digetsivo do Hospital Universitário Cassiano Antônio Moraes, da Universidade Federal do Espírito Santo, além de revisão de literatura nas bases de dados do Pubmed, para alertar a comunidade de atenção à saúde, principalmente médicos, sobre o fenótipo apresentado na Síndrome de Gardner, possibilitando o diagnóstico precoce.*

Palavras-chave | *Síndrome de Gardner; Polipose Adenomatosa Familiar; Desmóide; Osteoma.*

ABSTRACT | Introduction: Gardner's syndrome is a rare, autosomal dominant disease associated with the mutation of the *Adenomatous polyposis coli* (APC) gene, characterized by colonic polyposis with a histopathology compatible with adenoma, associated with mesenchymal tumor, such as desmoid type, osteomas and dental alterations. Extraintestinal manifestations may be the first findings, being important knowledge and disclosure of the clinical condition, allowing early diagnosis, adequate management and family investigation. **Case report:** This case report aims to describe the clinical case of familial adenomatous polyposis with a variant compatible with Gardner's Syndrome, in a patient with extra intestinal manifestations with desmoid tumor, supernumerary teeth and osteomas, ongoing at the Digestive System Unit of the Cassiano Antônio Moraes University Hospital, Federal University of Espirito Santo – Brazil, in addition to a literature review in the *Pubmed databases* to alert the health care community, especially doctors, about the phenotype presented in Gardner's Syndrome, enabling early diagnosis.

Keywords | Gardner Syndrome; Familial adenomatous polyposis; Desmoid; Osteoma.

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INTRODUCTION |

Gardner's Syndrome is a variant of Familial Adenomatous Polyposis (FAP), described in 1950s by Gardner and Plenk[1]. The prevalence of Gardner's Syndrome cannot be separated from FAP and general prevalence is 2.29 to 3.2 per 100.000 people in the world[3]. It has autosomal dominant inheritance and is characterized by colonic polyposis (more than 100 colon polyps), multiple osteomas and mesenchymal tumors. It relates to the mutation in the *Adenomatous polyposis coli* (APC) tumor suppressor gene, located on the long arm of chromosome 5 (5q21-q22), the mutation site of which determines the phenotype of the disease[4]. Most cases are due to family inheritance, but in one third of cases there is "*de novo*" mutation[4]. The formation of polyps begins at puberty, but the diagnosis usually occurs in the third decade of life and almost 100% will develop colorectal cancer by age 40[5]. Clinical findings include anemia, abdominal pain, diarrhea, abdominal mass, dental abnormalities and desmoid mesenchymal tumors[4].

We present the case of a 30 years old woman with colonic polyposis, cervical desmoid tumors, face osteomas and dental modifications. This case report was approved by the Research Ethics Committee with the ruling number 4.002.507.

CASE REPORT |

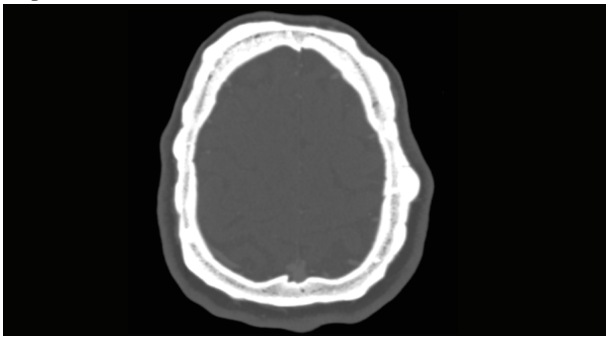
Thirty years old woman, single, childless and without previous gastrointestinal symptoms. She was referred to the gastroenterology department after a colonoscopy, which identified colonic and rectal adenomatous polyps with low grade epithelial dysplasia and tubular pattern. Examination was requested by a dental surgeon after finding supranumerary teeth during a routine orthodontic assessment.

She has a previous history of multiple exeresis of desmoid fibroids in the cervical region with local recurrences and report a family history of intestinal polyposis (mother and maternal uncles). During physical examination, was observed a hardened tumor in the frontal region and supranumeric teeth through oroscopy.

Based on the findings of the colonoscopy and physical examination, the hypothesis of Gardner's Syndrome was proposed and was oriented screening of siblings. She was referred to geneticist and her heredrogram is compatible with autosomal dominant inheritance, phenotype 175100 in the Online Mendelian Inheritance in Man (OMIM).

Skull tomography showed multiple dense bone lesions in the skull and jaw, consistent with osteomas (Figure 1) and the presence of supranumerary dental components inside the maxillary bone; thyroid ultrasound without lesions and upper digestive endoscopy with sessile polyps in the gastric fundus and multiple sessile polyps in the second duodenal portion, measuring 2 to 4 mm, with histopathological analysis compatible with polyps of fundal glands and tubular adenomas with low-grade dysplasia, respectively, compatible with Stage II of the Spigelman Classification (Table 1)[6].

Figure 1 - Dense bone lesions scattered through the skullcap compatible with osteomas



Source: Authors.

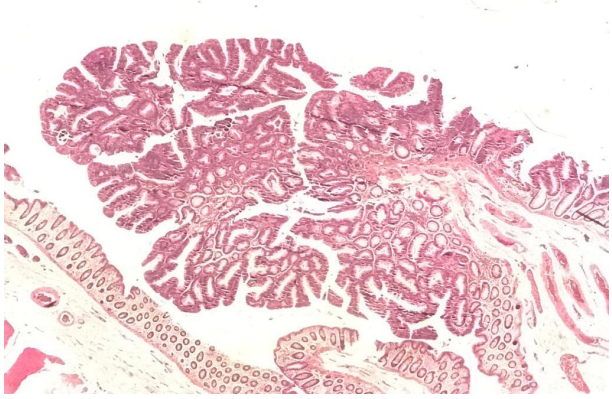
Table 1 - Spigelman Classification

	1 point	2 points	3 points
Number of polyps	< 4	5-20	>20
Polyp size	0-4 mm	5-10mm	>10mm
Histology	Tubular	Tubulovillous	Villous
Dysplasia	Low grade	Moderate grade	High grade

Stage 0: 0 points - Surveillance every 4 years; Stage I: 1-4 points - Surveillance every 2-3 years; Stage II: 5-6 points -Surveillance every 1-3 years; Stage III: 7-8 points - Surveillance every 6-12 months; Stage IV: 9-12 points - Surveillance every 3-6 months and surgery evaluation. (Spigelman AD, Williams CB, Talbot IC, Domizio P, Phillips RK.Upper gastrointestinal cancer in patients with familial adenomatous polyposis. Lancet 1989; 2(8666):783-5.)

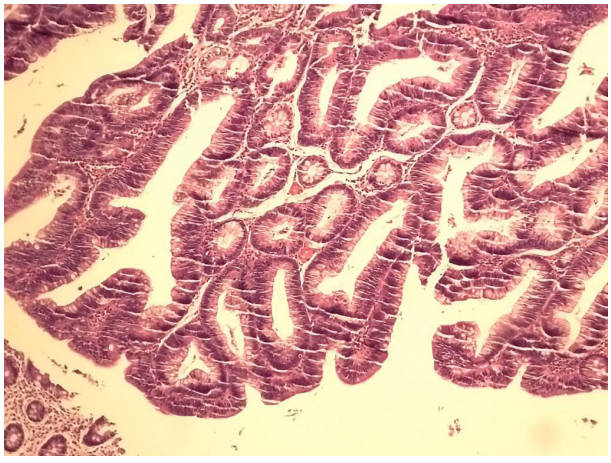
Submitted to total colectomy with ileorectal anastomosis, with no complications.The surgical specimen, 81 cm long and 3.5 to 5 cm in diameter, had brown and pleated mucosa with multiple tiny polyps, the largest measuring 0.7 x 0.6 cm. Histopathological analysis showed large intestine with tubular adenomas with atypical low-grade epithelium (Figure 2 and 3) and mesocolic fibromatosis and 50 lymph nodes with simple reactive state.

Figure 2 - Pediculated polyp protruding into large bowel lumen – adenomatous polyp. H&E; 20X



Source: Authors.

Figure 3 - Adenomatous polyp with low-grade epithelial dysplasia and tubular pattern– H&E; 100X



Source: Authors.

The patient maintains ambulatory follow-up, with periodic endoscopic evaluation of the remaining rectum, upper digestive endoscopy and thyroid ultrasound.

DISCUSSION |

Gardner's syndrome is a multisystemic disease and the diagnosis usually occurs at the age of 30[7]. Polyp formation begins at puberty, and, in addition to colonic involvement, gastrointestinal manifestations include gastric polyps of the fundic glands and adenomatous polyps of the duodenum and periampular region[5]. Spigelman Classification (Table 1) is used for duodenal polyps and is based on the number, size, histology and degree of dysplasia of polyps and defines the interval of performing upper digestive endoscopy for follow-up and the need for intervention. Gastrointestinal symptoms are nonspecific and may include constipation or diarrhea, abdominal pain, palpable abdominal masses and weight loss[4].

In general, bone abnormalities and skin manifestations appear 10 years before polyposis. Osteomas occur in half of the patients and are located mainly in the skull, predominantly the jaw and maxilla, and is often the reason for dental consultation. The most common skin lesions are desmoid cysts, sebaceous cysts, fibroids and lipomas[7].

Desmoid tumors occur in up to 7.5 -10% of patients and are benign lesions, but their progressive growth can lead to compression of gastrointestinal and urinary tract structures or nervous and vascular structures. There is possibly the development in the mesentery, retroperitoneum, abdominal wall or places of previous surgical approach[4]. Treatment is based on the size, symptoms and behavior of tumor growth. Treatment can be chemotherapy, radiotherapy and surgery, with up to 80% recurrence[7].

Other manifestations include hypertrophy of the pigmented epithelium of the retina present in 90% of patients with FAP and characterized by hyperpigmented oval areas at the funduscopic examination and dental changes, such as supranumeric teeth, odontomas and impacted teeth, observed in 70% of patients[7].

Colorectal Carcinoma (CRC) occurs in almost 100% of patients who have not undergone prophylactic colectomy until age 40. The second most common cause of death in this patients, after CCR, is duodenal/periampullary carcinoma, occurring in approximately 5-6% of the patients. Other neoplasms are pancreatic adenocarcinoma (2%), papillary thyroid cancer (2%), gastric adenocarcinoma (0.5%) and hepatoblastoma in children younger than five (1.6%)[4].

The diagnosis of Gardner's syndrome is based on the colonoscopy finding of colonic polyposis, in addition to clinical findings and positive family history[4]. Whenever possible, the clinical diagnosis should be confirmed by genetic testing. After the diagnosis of Gardner's Syndrome, as well as other variants of FAP, patients should follow up with an annual colonoscopy, upper digestive endoscopy between ages 20 to 25 and afterwards with a frequency established according to the Spigelman Classification[7] and annual thyroid ultrasound starting between age 15 and 20[8]. Desmoid tumors should be investigated with imaging tests, if palpable mass or symptoms occur[8].

For the prevention of CRC, for all patients with FAP, regardless of subtype, prophylactic colectomy is indicated, usually between age 15 and 25. Surgical options are colectomy with ileorectal anastomosis, total proctocolectomy with ileostomy and proctocolectomy with or without mucosectomy with ileal pouch anal anastomosis[4]. The definition of the type of surgery depends on the amount of colonic polyps, the amount of rectal polyps, the degree of dysplasia and the presence of CRC. In case of surgery with the remaining rectum, annual evaluation is indicated for removal of adenomas that may recur[5].

For chemoprevention, studies show benefits with the use of nonsteroidal anti-inflammatory drugs, such as Sulindac and Celecoxib, aimed reduction in the number and size of polyps during the period of their administration[7].

CONCLUSION |

We present the case of a patient with the common age for FAP diagnosis, a phenotype compatible with Gardner's Syndrome, presenting desmoid tumors, osteomas and supranumeric teeth, with positive family inheritance, submitted to total colectomy with ileorectal anastomosis, with annual monitoring with rectoscopy and thyroid ultrasound and upper digestive endoscopy every 1 to 3 years, as defined by the Spigelman Classification.

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