

Case Report

A Case Report of Gardner's Syndrome and a Review of Literature

Mitra Heidarpour¹, Seyed Abass Tabatabai², Majid Heidarpour³, Farzaneh Sajjadi¹

1. Dept. of Pathology, Isfahan University of Medical sciences, Isfahan, Iran

2. Dept. of Surgery, Isfahan University of Medical sciences, Isfahan, Iran

3. Dept. of Orthodontics, Shahid Beheshti University of Medical Sciences, Tehran, Iran

ABSTRACT

Gardner's syndrome is an autosomal dominant inherited disorder. Familial polyposis of the colon, osteomas, hypertrophy of the retinal-pigmented layer and a multitude of soft tissue tumors are characteristic features. The syndrome may be presented with colonic or extracolonic symptoms. A 75-year-old male patient presented to Al-zahra Clinic with diffuse abdominal pain. An abdominal surgery was performed on him due to invasive abdominal mass. The surgical specimen was examined by H&E and immunohistochemical staining. The final diagnosis was fibromatosis. There was a history of gardner's syndrome in his family. Colonoscopy was done to confirm the diagnosis of gardner's syndrome. The diagnosis of gardner's syndrome was made according to following findings: abdominal fibromatosis, multiple jaw osteomas and polyposis coli. The patient with gardner's syndrome can present with abdominal fibromatosis even in an old age. In IHC staining CD117 was seen with coarse granular cytoplasmic pattern in fibromatosis, and so, this pattern of CD117 staining can be a clue to the diagnosis of fibromatosis.

Key words: Gardner's Syndrome, Familial Polyposis Coli, Abdominal Fibromatosis, Iran

Introduction

Gardner's syndrome (GS) is a dysplasia characterized by neoformations of the intestine, soft tissue, and osseous tissue (1). It is a rare autosomal dominant inherited disorder with a high degree of penetrance characterized by the triad of colonic polyposis, multiple osteomas and mesenchymal tumors of the skin and soft tissues including epidermal inclusion cyst, lipoma, fibroma, and fibromatosis (2-4) It is classified as one of familial adenomatous polyposis (FAP). The diagnosis of this disease is often delayed because the patients present

with very different symptoms (5).

In 1952, Gardner and Plenk reported the condition of multiple osteomas associated with colonic polyposis inherited with a dominant pattern (6). Later, Gardner and Richards described Gardner's syndrome, i.e. hereditary colonic polyposis associated with osteomatosis and multiple cutaneous and subcutaneous tumors (7).

The mutated gene in these patients is APC gene. Although most cases show familial clustering, one-third of cases occur due to spontaneous mutations. More than 1400 different mutations of APC gene have

Received: 6 October 2010

Accepted: 3 January 2010

Address communications to: Dr Mitra Heidarpour, Department of Pathology, Isfahan University of Medical sciences, Isfahan, Iran

Email: heidarpour@med.mui.ac.ir

been found in these patients and the type of mutation affects the extracolonic manifestations as well as number, malignant potential and time of presentation of colonic polyps(5). Because of variable expression of adenomatous polyposis coli (APC) gene mutations associated with GS, a wide range of phenotypes are observed clinically, with some patients having few soft-tissue lesions(8). The presence of desmoid fibromatoses, normally uncommon in young patients, should signal the presence of underlying Gardner's syndrome (9-12).

Case Report

A 75-year old male patient presented with a large intra-abdominal mass. After careful clinical examination a hypogastric mass was detected that extended to umbilical area. The mass was fixed, nontender and had a firm consistency. According to the patient history, the abdominal tumor size increased rapidly during the previous 6 months. In CT scan, presumptive diagnosis of sarcoma was made, and the abdominal laparotomy was performed and an ill-defined 20 cm mass with a firm consistency and a white trabecular surface with extension to intra abdominal viscera were detected on surgery. On microscopic examination a fibroblastic proliferation with fascicular pattern and abundant collagen bundles, rare mitotic activity and delicate thin walled compressed vessels were detected (Fig.1). Immunohistochemical staining was performed on the specimen and vimentin was strongly positive and CD117 was positive with coarsely cytoplasmic pattern (Fig. 2). Beta-catenin was positive with a nuclear pattern but actin, desmin, S-100 and CD34 were negative. The final report was that of fibromatosis.

There was a history of gardner's syndrome in his family. Therefore, colonoscopy was performed for this patient and on colonoscopy, he had numerous polyps covering colon and rectum, suggestive for the diagnosis of familial adenomatous polyposis (FAP).On biopsy, adenomatous polyps with moderate to severe dysplasia without stromal invasion was detected. An upper endoscopy was performed with normal findings. No surgery was performed because

of patient's age and instead, follow-up with periodic colonoscopy was planned. The patient was referred to different disciplines for complete check up and multiple jaw osteomas were detected on skull view (Fig.3). He had also numerous supernumerary teeth especially in mandibular molars area. The patient did not have any ophthalmologic exam in his history before presentation with abdominal symptoms. On discharge, it was recommended that the patient and all his first-degree family members should be evaluated for FAP but the patient refused genetic counseling, nevertheless all other five family members of the patient had their genome evaluated and FAP had been confirmed. We were not able to follow the patient for the results because the patient's address was changed.

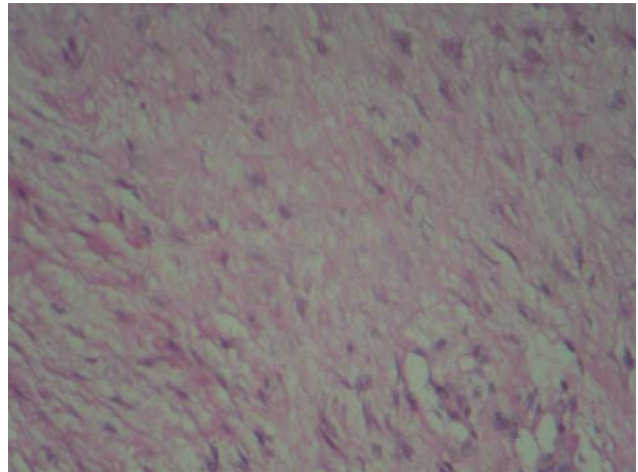


Fig. 1: microscopic view of the desmoid sample (H&E \times 400)

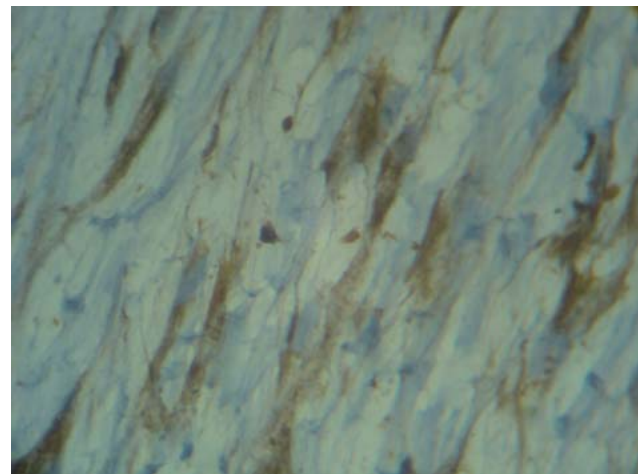


Fig. 2: Diffuse strong cytoplasmic staining for c-Kit in the desmoid sample with the A4502 antibody (\times 400)



Fig. 3: Skull view shows multiple jaw osteomas

Discussion

Gardner's syndrome is a disease that affects multiple systems. Symptoms are usually present by the end of 2nd decade of life, but they may present anytime between 2 months and 70 years (1,3,12). In our case, the patient presented with abdominal fibromatosis in an old age (75 years old) without any significant prior history related to his disease although remaining symptomless until this old age is rare. The gastrointestinal manifestations of this disease are as follows: colonic adenomatous polyps (tubular, villous, tubulovillous), gastric and small intestinal adenomatous polyps (12% of patients) and peri-ampullary carcinomas (2% of patients). In most patients, polyps form at puberty for the first time but the condition is diagnosed in the third decade, and by the fourth decade, malignant transformation has happened in all patients (5). Despite, our case did not have malignant transformation of colonic polyps even in the 7th decade of his life and polyps were asymptomatic at the time of diagnosis. Prophylactic colectomy is indicated (13, 14), although desmoid tumors of the mesenteric and abdominal wall may develop after surgery (5, 15, 16). Most of the polyps are small (<5 mm). The larger polyps may lead to intussusception (5). In consultation with GI surgery department, long-term follow up with colonoscopy, without performing colectomy due to the patient's age and the risk of surgery, was confirmed as the best treatment option for this patient.

Oral and maxillofacial symptoms of GS include an increased risk of jaw osteomas, odontomas and supernumerary or unerupted teeth. Several studies have assessed the occurrence of osteomas in FAP patients and control subjects (17). In one study (17), the incidence of osteoma in FAP was 4 to 20 times more frequent than in control group. Most osteomas are asymptomatic. Nevertheless, some patients complain about large hard swellings at the angle of the mandible (17). The osteomas are endosteal or exosteal and may cause deformity (5). The site of most osteomas is on the skull. In the skull, the most common sites are maxilla and mandible and so, many patients present to oral and maxillofacial surgeons for the first time. However, long bones and even phalanges may be affected. Finding of three or more osteomas is suggestive for Gardner's syndrome (2, 18, 19). As it is shown in the previous part, our patient had multiple osteomas in the jaws (consistent with the general pattern of these patients), and the supernumerary teeth were in the molar region although typically supernumerary teeth are in the lower premolar region.

Deep fibromatosis is a locally aggressive but not metastasizing proliferation. Intra-abdominal fibromatosis (IAF) occurs either in association with Gardner's syndrome or as a sporadic event and presents in most cases differential diagnostic problems with myofibroblastic or fibroblastic tumors, characterized by a more aggressive biological behavior such as gastrointestinal stromal tumors (GISTs). In absence of regional and/or distant metastasis, differential diagnosis may be difficult and represents a topical issue, since it influences treatment choice. Fibromatosis is particularly likely to be misdiagnosed as GIST because it can extensively involve the gastrointestinal wall and exhibit CD117 immunoreactivity although the latter tends to be exclusively cytoplasmic and not on the cell membrane. Fibromatosis have been reported to be c-kit (CD117) positive in several studies (20-22), although some studies report this staining as a nonspecific pattern rather than true positivity (23) and others report that the results of this staining has been different based on the type of antibody used for

it (23, 24). In our case, the gastrointestinal viscera were extensively involved with the abdominal tumor and so GIST was considered as one of the first differential diagnoses. Therefore, we evaluated our specimen with c-kit and beta-catenin antibodies and coarsely cytoplasmic positivity of c-kit and nuclear positivity of beta-catenin confirmed the diagnosis of fibromatosis.

Other manifestations of Gardner's syndrome are papillary thyroid carcinoma, benign intracranial meningiomas, benign intracranial epidermoid cysts, osteosarcoma, chondrosarcoma, leiomyomas, hepatoma, hepatoblastoma, fibromas, lipomas, biliary and adrenal neoplasms (5). None of these other rare tumors were detected in the multidisciplinary evaluation performed for this patient.

Acknowledgements

The authors declare that they have no conflicts of interest.

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