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*Case Report*

# Gardner syndrome with a giant mass in the thoracic cavity: a case report and analysis of the related complications

Dehui Yang[1*], Xianghao Zeng[1*], Yipin Lv[1*], Weilin Liao[2], Shanhong Tang[1], Jianqin Jiang[2]

*Departments of [1]Digestive Diseases, [2]Thoracic Surgery, General Hospital of Western Theater Command, Chengdu 610083, Sichuan, China. [*]Equal contributors.*

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**Abstract:** Gardner syndrome (GS) is a form of familial adenomatous polyposis (FAP) and is characterized by colonic polyposis, osteomas, and soft-tissue tumors. Desmoid tumors (DT) are lesions of mesenchymal origin and are an extra-colonic manifestation of GS. Gardner-associated fibroma (GAF) is considered to be a benign soft-tissue lesion related to DT and FAP. Here we present a case of an 18-year-old female patient with a huge lump in her right thoracic cavity and another lump located in her left lumbar muscles who was diagnosed with GS through a colonoscopy and through *adenomatous polyposis coli* (*APC*) gene mutation detection. The patient underwent a surgical resection of the right thoracic tumor. Three months later, the left waist lump underwent medical treatment with tamoxifen and celecoxib and was monitored using computed tomography (CT). Subsequently, colonoscopy screening was performed annually to prevent colorectal cancer. GAF is frequent in GS, and such a huge GAP in the thorax is very rare, with few cases reported in the literature. Patients with GS must be closely monitored, and clinical and imaging examinations must be performed to detect any signs of tumors.

**Keywords:** Gardner syndrome, familial adenomatous, desmoid tumor, case report

## Background

Familial adenomatous polyposis (FAP) is an autosomal dominant disease caused by *adenomatous polyposis coli* (*APC*) gene mutations. This genetic disorder causes extensive polyps of the colon and rectum and is likely to develop into colon cancer in patients who do not undergo prophylactic colectomy [1].

Gardner syndrome (GS), a variant of FAP, has particularly prominent intestinal lesions, but various extra-colonic manifestations may occur, such as osteomas, skin tumors, and desmoid tumors (DT) [2]. The WHO diagnostic criteria for GS conform to three conditions: (1) ≥100 colorectal polyposis (adenoma); (2) *APC* gene germline mutation; (3) a family history of FAP, and at least one epidermoid cyst, osteoma, or DT [3]. Extra-colonic manifestations frequently occur before intestinal manifestation. The WHO defines DT as a clonal proliferation of fibroblasts that arises in the deep soft tissues and is characterized by infiltrative growth and a tendency toward local recurrence but an inability to metastasize [4]. According to relevant studies, 7.5%-16% of FAP patients have DT [5], a lesion of mesenchymal origin [6]. DT predominantly occurs in females from puberty to 40-years-old. Vimentin is strongly positive in DT cells, and myosin smooth muscle actin (MSA) and smooth muscle actin (SMA) are positive in varying degrees. GAF is a benign soft-tissue lesion with fibroblasts randomly distributed in thick collagen bundles. Vimentin and CD34 are positive in the spindle cells of GAF, but MSA and SMA are negative [4]. Generally, DT and GAF are asymptomatic. The threat depends on tumor size and anatomic site. They are similar in microstructure and immunohistochemistry. GAF is considered a precursor of DT, which is a benign lesion, and GAF also plays a potential sentinel role for FAP [7, 8].

## Case presentation

An 18-year-old female experienced chest pain after exercising but did not seek medical advice

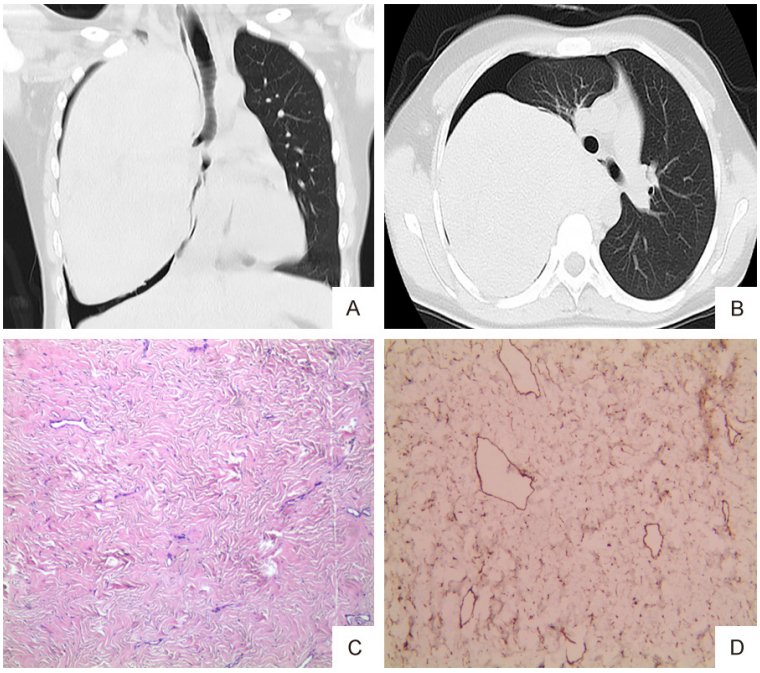


**Figure 1.** A and B. The tumor (23.2 × 13.3 × 13.1 cm) occupied the right thoracic cavity, the right lung was compressed to 20%, and the mediastinum moved to the left. C. Pathological H&E staining showing GAF. D. Immunohistochemistry images showing CD34$^+$ (brown) cells infiltrating the GAF.

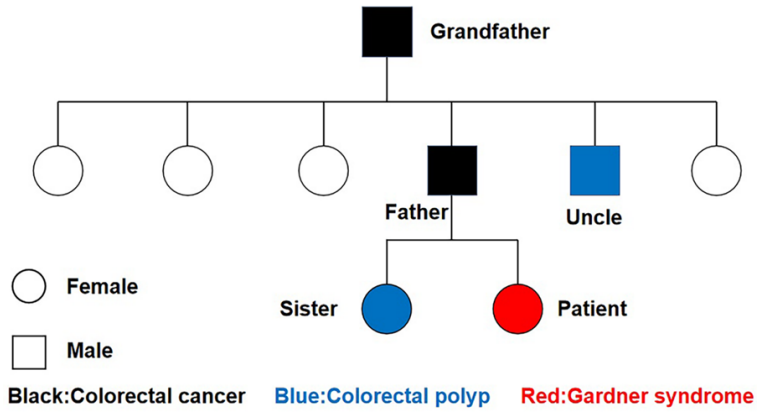


**Figure 2.** Family tree: the patient's grandfather and father died of colorectal cancer. The patient's sister and uncle had multiple colorectal polyps. Her uncle underwent a colorectal resection.

immediately. Prior to her visit, her symptoms gradually worsened over the previous three months. The patient was transferred to our hospital from the local hospital. Further chest computed tomography (CT) indicated a huge mass on the right thoracic cavity and a compression of the right lung tissue (**Figure 1A** and **1B**). A retrospective family history revealed that the patient's father and grandfather died of colon cancer, and her sister and uncle suffered from multiple polyps (**Figure 2**).

The thoracic mass biopsy was suggestive of GAF (**Figure 1C**), and immunohistochemical staining indicated CD34$^+$ cells infiltrating in GAF (**Figure 1D**). GS was considered after a multidisciplinary consultation. Next, an endoscopy revealed multiple polyps in the digestive tract (**Figure 3A**), and a rectal polyp biopsy indicated tubular adenoma (**Figure 3B**). APC gene mutation screening showed a deletion mutation at exon15 (c.4612_4613delGA (p.Glu1538Ilefs*5)) (**Figure 4**). According to the WHO diagnostic criteria, the patient was diagnosed with GS. Further examination using abdominal magnetic resonance imaging (MRI) showed another mass in the left lumbar muscles (**Figure 5A**), and a pathological examination suggested that the striated muscle bundles atrophied, and thick bundles of collagen permeated between the muscle bundles, and the fibroblasts were locally scattered (**Figure 5B**).

The patient underwent a surgical resection of the right thoracic tumor. The tumor occupied more than 70% of the right thoracic cavity, and part of the tumor invaded the left thoracic cavity. It originated at the upper end of the right chest wall near the spine. A postoperative chest CT showed a good recovery of the lung.

Three months later, the patient went to our hospital again for the left waist tumor resection. Positron emission computed tomography (PET) showed an irregular and slightly high density tumor with slightly elevated 18F-fludrodeoxyglucose (FDG) metabolism in the left quadra-

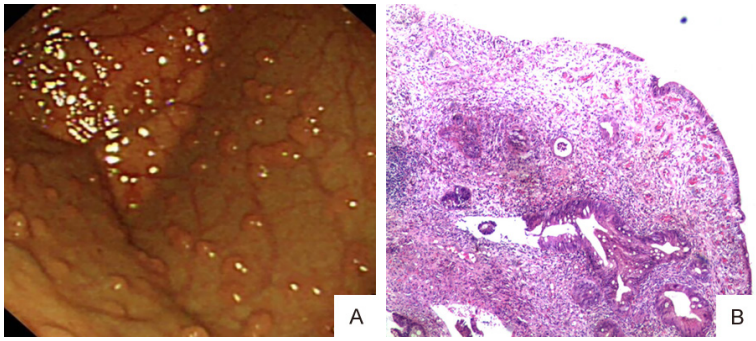

**Figure 3.** A. The endoscopic findings showed multiple polyps in the colon, stomach and duodenum. B. A rectal polyp biopsy revealed a tubular adenoma (8 cm from the anus).

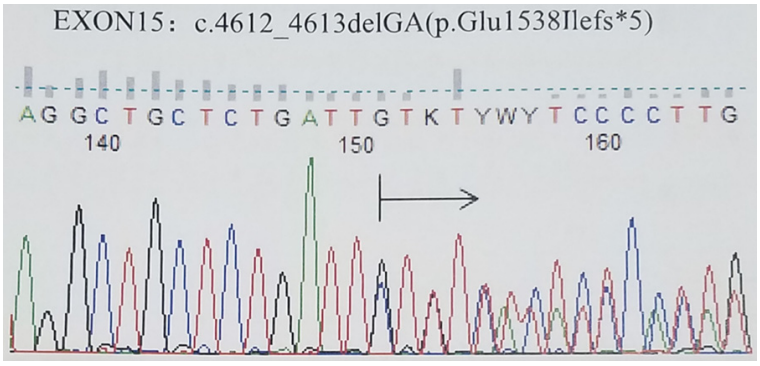


**Figure 4.** Deletion mutation of *APC* exon15 (c.4612_4613delGA (p.Glu1538Ilefs*5)). The mutation lead a frameshift mutation that caused the coding protein to terminate prematurely.

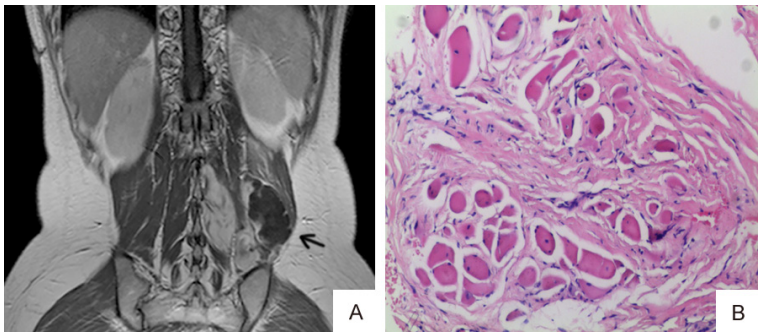

**Figure 5.** A. An MRI showing heterogeneous signals in the left lumbar dorsal muscles and unclear boundaries with adjacent tissues. The arrow points to a mass on the left lumbar spine. B. The H&E staining showed the striated muscle bundles atrophied, and thick bundles of collagen permeated between the muscle bundles and fibroblasts scattered locally.

tus lumbago and the left erector spinae (L3-5 vertebral plane), suggesting malignant lesions (originating from the mesenchymal tissue) with hemorrhaging. The biopsy of the tumor showed a coincidence with the DT (**Figure 5B**). After the second multidisciplinary consultation, the surgical resection was abandoned due to the tremendous risk and serious complications. According to relevant studies [5, 9], the combination of tamoxifen and celecoxib was selected as the drug therapy for the DT, which was monitored by CT follow-up. Further colonoscopies are to be performed annually to prevent colorectal cancer.

## Discussion

From the available reports, we have never seen such a huge GAF in the thoracic cavity. GAF often appears earlier than polyps and prefers childhood and young adulthood, which is closely related to the FAP/*APC* gene mutation [8]. According to recent studies, GAF might be a sentinel marker of FAP [7, 10]. The early warning of GAF is especially important among the probands of novo mutation. These patients tend to have a negative family history. GAF is also associated with the occurrence of DT, but the mechanism is still unclear. Both are closely related to *APC* mutation. Moreover, DT is also associated with trisomy 8 and 20 or catenin beta-1 (*CTNNB1*) [4, 11, 12].

According to Caspari et al, the *APC* gene mutation between codon 1445-1578 is related to the susceptibility of DT [13]. But in a recent study, the Voytek team emphasized that the *APC* gene mutation between codons 543-713 and 1310-2011 was related to an increased risk of DT [14]. Studies on DT and *APC* gene mutations are continuing. The genetic research on FAP and its related soft-tissue tumors is progressing. We expect that genetic testing will be able to be used to evaluate the prognosis and monitor FAP and its related soft-tissue tumors in the future.

At present, surgery remains the first choice for DT treatment [5]. When surgical resection is not appropriate, patients can choose cryoablation, radiotherapy, or drug therapy [9]. Drug therapy is more acceptable to patients than invasive treatment. Because of rare adverse events and their low cost, anti-hormonal agents such as tamoxifen are used alone or in combination with nonsteroidal anti-inflammatory drugs (NSAIDs) as the first treatment [9, 15, 16]. In addition, targeting the notch signaling pathway is a new therapeutic strategy in patients with refractory progressive DT [17]. However, some prospective studies have shown that imatinib, a tyrosine kinase inhibitor (TKI), has a high stability rate (60%-80%) and a low response rate (6%-16%) for progressive DT [18-20]. We still believe that there will be additional effective targeted drugs for DT treatment.

GS is a rare but serious dominant inherited syndrome. Once the disease has occurred, long-term monitoring and treatment need to be carried out. A colonoscopy is required every 1-2 years. The risk of colorectal cancer approaches 100% when a patient is older than 50 [1]. It is a heavy financial and psychological burden for patients and their families. However, in clinical practice, the ability to diagnose GS is still limited. Some patients with extra-colonic symptoms are often overlooked or misdiagnosed. We hope that this article will draw more attention to FAP and related soft-tissue tumors.

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Informed consent for the publication of the data was obtained from the patient.

## Disclosure of conflict of interest

None.

## Abbreviations

APC, Adenomatous polyposis coli; CT, Computed tomography; DT, Desmoid tumor; FAP, Familial adenomatous polyposis; FDG, 18F-fludrodeoxyglucose; GAF, Gardner-associated fibroma; GS, Gardner Syndrome; MRI, Magnetic resonance imaging; MSA, Myosin smooth muscle actin; PET, Positron emission computed tomography; SMA, Smooth muscle actin.

**Address correspondence to:** Shanhong Tang, Department of Digestive Diseases, General Hospital of Western Theater Command, Chengdu 610083, Sichuan, China. E-mail: shanhongtang@163.com; Jianqin Jiang, Department of Thoracic Surgery, General Hospital of Western Theater Command, Chengdu 610083, Sichuan, China. E-mail: Liuwei_52-0520@126.com

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