

# Gardner's Syndrome — Emphasis on Desmoid Tumors

Kuo-Chih Tseng, Chih-Wen Lin<sup>1</sup>, Jeh-En Tzeng<sup>2</sup>, Wei-Feng Feng, Yu-Hsi Hsieh, An-Liang Chou, Chang-An Tseng

Department of Internal Medicine, Radiology<sup>1</sup>, Pathology<sup>2</sup>, Buddhist Dalin Tzu Chi General Hospital, Chiayi, Taiwan

## ABSTRACT

Desmoid tumors are uncommon benign neoplasms of fibroblasts in familial adenomatous polyposis / Gardner's syndrome. The mesentery of the small bowel is the first frequently involved site of desmoid tumors. Herein, we report a 25 year-old woman with Gardner's syndrome complicated by desmoid tumors over the mesentery, abdominal wall and the paraspinal area, which resulted in obstructions of the small bowel and upper urinary tract. Total parenteral nutrition was administered, but she finally died of malnutrition and sepsis fourteen months after diagnosis. (*Tzu Chi Med J* 2006; **18**:57-60)

*Key words:* Gardner's syndrome, familial adenomatous polyposis, desmoid tumor

## INTRODUCTION

Gardner's syndrome (GS) is an autosomal dominant inherited disease, characterized by polyposis coli, osteoma, and various soft tissue tumors, including desmoid tumors [1,2]. Desmoid tumors are benign neoplasms of fibroblasts characterized by local invasiveness. They often recur after surgical resection. They constitute about 3.5% of all fibrous tissue tumors and 0.03% of all neoplasms [3]. In addition to the extremities and trunk, desmoid tumors often arise in the abdominal wall and the mesentery, leading to obstruction of the intestine and urinary tract. We here introduce a case of GS complicated by desmoid tumors over the mesentery, abdominal wall and the paraspinal area, which resulted in obstructions of the small bowel and upper urinary tract.

## CASE REPORT

A 25 year-old woman came to Dalin Tzuchi hospi-

tal with chief complaints of postprandial vomiting and body weight loss for one year. The patient was in her usual state of health until three years previously when mesenteric desmoid tumors were diagnosed. She had two surgeries at another hospital, three years before and one year before this admission. Residual tumors and short bowel syndrome were noted after the operations. During the past year, she suffered from intermittent episodes of vomiting and poor intake, followed by marked weight loss. On admission, physical examination revealed a cachectic look without acute distress. A palpable hard mass about 10 × 5 cm was detected over the right lower quadrant of the abdomen. Panendoscopy showed polyposis of the stomach, especially in the fundic region (Fig. 1A) and in the duodenum. Gastric biopsy specimens revealed fundic gland polyps (Fig. 2A). Colonoscopy revealed polyposis of the colon, especially in the rectosigmoid colon (Fig. 1B). The pathology showed tubular adenoma (Fig. 2B). Computed tomography of the abdomen showed diffuse masses and nodules in the abdominal wall, mesentery, and paraspinal area (Fig. 3). A dilated bowel and bilateral hydronephrosis were also noted,

Received: October 4, 2005, Revised: November 1, 2005, Accepted: December 26, 2005

Address reprint requests and correspondence to: Dr. Kuo-Chih Tseng, Department of Internal Medicine, Buddhist Dalin Tzu Chi General Hospital, 2, Min Sheng Road, Dalin, Chiayi, Taiwan

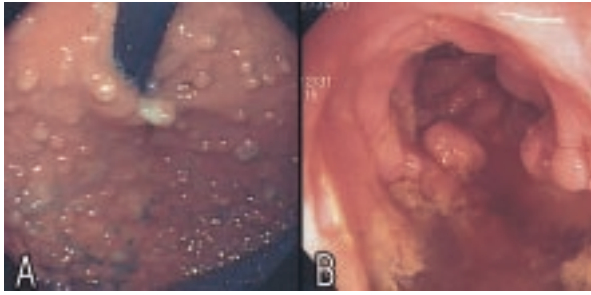


Fig. 1. (A) Panendoscopy shows multiple sessile polyps over the fundus, measuring about 0.2-0.3 cm. (B) Colonoscopy reveals multiple polyps of various sizes over the colon, mainly in the rectosigmoid colon.

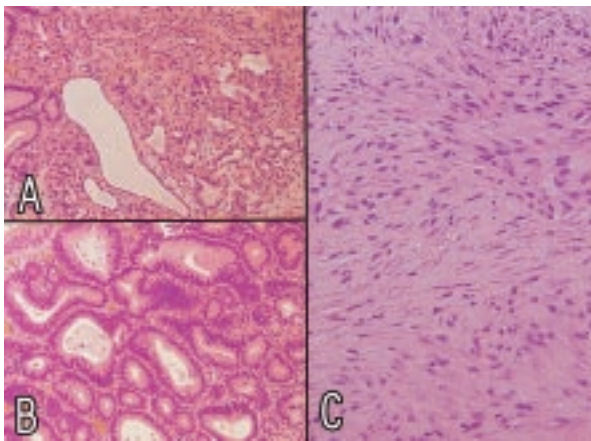


Fig. 2. (A) The pathology of the gastric polyps reveals fundic gland polyps with dilated lumens (H&E 100 $\times$ ). (B) The pathology of the colonic polyps reveals tubular adenoma (H&E 100 $\times$ ). (C) The pathology of the mass in the right lower quadrant of the abdomen discloses proliferating spindle cells with a whirling storiform picture, compatible with fibromatosis (H&E 200 $\times$ ).

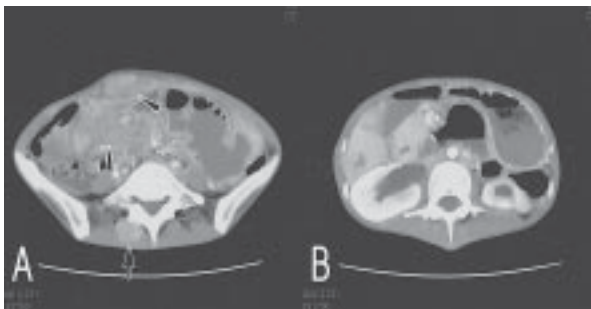
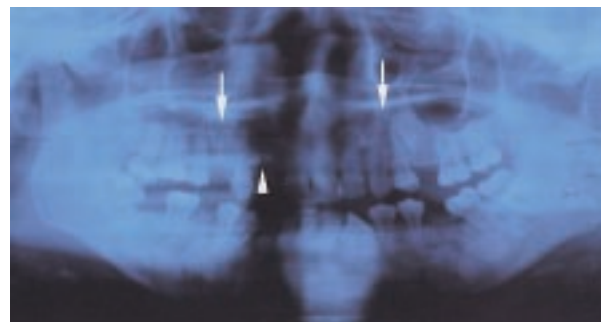


Fig. 3. (A) Computed tomography of the abdomen discloses desmoid tumors over the abdominal wall (arrowhead), the mesentery (double arrowhead) and the paraspinal area (arrow). (B) Desmoid tumors of the mesentery resulting in bowel obstruction and bilateral hydronephrosis.

implying obstructions of the intestine and upper urinary tract. Ultrasound-guided biopsy of a mass in the right lower quadrant of the abdomen revealed proliferating spindle cells with a whirling storiform picture, favoring fibromatosis (Fig. 2C). Based on the above manifestations, GS was diagnosed. Further evaluation showed osteoma over the cranial bone (Fig. 4A). There were also odontomas and a supernumerary tooth on a radiograph of the maxilla and mandible (Fig. 4B). Surgery was not suggested due to multiple involvement of desmoid tumors in the mesentery. Chemotherapy and radiotherapy were suggested, but the family refused. Tamoxifen and celecoxib were administered, but with poor effect partly because of intestinal obstruction and short bowel syndrome. Total parenteral nutrition was



A



B

Fig. 4. (A) Computed tomography of the brain shows a small osteoma over the left frontal bone. (B) Odontomas (arrow) and a supernumerary tooth (arrowhead) are present on radiography of the maxilla and mandible.

administrated for long-term nutritional support. In spite of aggressive nutritional support, the patient died of malnutrition and sepsis fourteen months after diagnosis.

## DISCUSSION

GS is inherited as an autosomal dominant disorder. It was first reported by Gardner and Smith in 1958. It is comprised of a triad of polyposis coli, osteoma, and various soft tissue tumors, including desmoid tumors [1,2].

Desmoid tumors are histologically defined as fibromatosis arising from the musculoaponeurotic soft tissues, and are composed of well-differentiated and uniform collagenous fibroblasts and fibrocytes. They are locally invasive but do not metastasize. Desmoid tumors are rare, accounting for 3.5% of all fibrous tissue tumors and 0.03% of all neoplasms [3]. These tumors develop in 10% to 18% of patients with familial adenomatous polyposis (FAP) [4-7]. About two percent of desmoid tumors are FAP-associated and patients with FAP have a risk of developing desmoid tumors 852 times that of the general population [8].

Although their roles are unclear, three factors, initiation of trauma, influence of sex steroids and an underlying genetic defect, have been implicated in the etiology of desmoid tumors [9]. In FAP, sixty-eight to eighty-six percent of intra-abdominal and abdominal wall desmoid tumors occur after abdominal surgery, especially within the first five years [9]. Despite the strong association with previous surgery, intra-abdominal desmoid tumors can occur spontaneously in FAP, and can even be the initial manifestation of FAP, such as in our patient [10]. There is a higher incidence of desmoid tumors in females, particularly in those of reproductive age, which supports the idea that the estrogen can stimulate desmoid growth. Some reports show that the desmoid tumors can be treated successfully by anti-estrogen drugs, implying a possible role of sex hormones in the disease [11,12]. From a genetic point of view, FAP can be considered a generalized disorder of tissue growth regulation caused by germline mutation in the *APC* gene. There is evidence of genotype-phenotype correlation in FAP. Desmoid tumors have been reported to occur frequently in patients with mutations beyond codon 1444 [13].

Desmoid tumors can be asymptomatic initially and found incidentally during examination or surgery. Intra-abdominal desmoid tumors cause small bowel obstruction, hydronephrosis, bowel perforation, enterocutaneous fistula and intestinal hemorrhage [14]. In our patient, the enlarged intra-abdominal desmoid

tumors caused small bowel obstruction and bilateral hydronephrosis, followed by failure of nutritional intake, leading to cachexia.

Based on their location, desmoid tumors can be divided into three types, intra-abdominal, abdominal wall and extra-abdominal, in order. In intra-abdominal desmoid tumors, the small bowel mesentery is the most commonly involved site, followed by the pelvic retroperitoneum and mesocolon [14]. In our case, the desmoid tumors involved the small bowel mesentery and abdominal wall.

Treatment is controversial, empirical and difficult. It is based largely on anecdotal reports and small, poorly controlled studies of predominantly sporadic desmoids [9]. Although surgery is widely accepted as the first line treatment for desmoid tumors, the high recurrence rate has led some authors to suggest that surgery be avoided except for bypass of bowel obstructions or relief of ureteric obstructions [4,9]. Pharmacological treatment with non-steroid anti-inflammatory drugs and anti-estrogen agents is the most widely documented management. Sulidac and tamoxifen are the two major drugs in clinical use [11,15]. Chemotherapy and radiotherapy are also two alternative treatments and should be considered in symptomatic patients who don't respond to conventional medical therapy [16-19]. In our case, surgery was not suggested due to multiple involvement of desmoid tumors in the mesentery. It was possible that surgery had failed to debulk these tumors completely. Pharmacological therapy with non-steroid anti-inflammatory drugs and tamoxifen failed, due partly to the equivocal effect of non-steroid anti-inflammatory drugs and tamoxifen or resistance to those two kinds of drugs. It was also possible partly due to total small bowel obstruction and short bowel syndrome.

In conclusion, desmoid tumors of the abdomen in FAP/GS are uncommon benign neoplasms of fibroblasts and can cause serious complications, including intestinal obstruction. Careful evaluation and management are mandatory.

## REFERENCES

1. Gardner EJ: A genetic and clinical study of intestinal polyposis, a predisposing factor for carcinoma of the colon and rectum. *Am J Hum Genet* 1951; **3**:167-176.
2. Smith WG: Multiple polyposis, Gardner's syndrome, and desmoid tumors. *Dis Colon Rectum* 1958; **1**:323-332.
3. McAdam WF, Goligher JC: The occurrence of desmoids in patients with familial polyposis coli. *Br J Surg* 1970; **57**:618-631.
4. Jones IT, Jagelman DG, Fazio VW, Lavery IC, Weakley

- FL, McGannon E: Desmoid tumors in familial polyposis coli. *Ann Surg* 1986; **204**:94-97.
5. Reitamo JJ, Scheinin TM, Haeyry P: The desmoid syndrome: New aspects in the cause, pathogenesis, and treatment of the desmoid tumor. *Am J Surg* 1986; **151**: 230-237.
  6. Penna C, Tiret E, Parc R, et al: Operation and abdominal desmoid tumors in familial adenomatous polyposis. *Surg Gynecol Obstet* 1993; **177**:263-268.
  7. Doi K, Iida M, Kohrogi N, et al: Large intra-abdominal desmoid tumors in a patient with familial adenomatous coli: Their rapid growth detected by computerized tomography. *Am J Gastroenterol* 1993; **88**:595-598.
  8. Gurbuz AK, Giardiello FM, Petersen GM, et al: Desmoid tumors in familial adenomatous polyposis. *Gut* 1994; **35**: 377-381.
  9. Clark SK, Phillips RK: Desmoids in familial adenomatous polyposis. *Br J Surg* 1996; **83**:1494-1504.
  10. Richards RC, Rogers SW, Gardner EJ: Spontaneous mesenteric fibromatosis in Gardner's syndrome. *Cancer* 1981; **47**:597-601.
  11. Sportiello DJ, Hoogerland DL: A recurrent pelvic desmoid tumor successfully treated with tamoxifen. *Cancer* 1991; **67**:1443-1446.
  12. Wilcken N, Tattersall MH: Endocrine therapy for desmoid tumors. *Cancer* 1991; **68**:1384-1388.
  13. Caspari R, Olschwang S, Friedl W, et al: Familial adenomatous polyposis: Desmoid tumors and lack of ophthalmic lesion (CHRPE) associated with APC mutations beyond codon 1444. *Hum Mol Genet* 1995; **4**: 337-340.
  14. Clark SK, Neale KF, Landgrebe JC, Phillips RK: Desmoid tumors complicating familial adenomatous polyposis. *Br J Surg* 1999; **86**:1185-1189.
  15. Belliveau P, Graham AM: Mesenteric desmoid tumor in Gardner's syndrome treated by sulindac. *Dis Colon Rectum* 1984; **27**:53-54.
  16. Schnitzler M, Cohen Z, Blackstein M, et al: Chemotherapy for desmoid tumors in association with familial adenomatous polyposis. *Dis Colon Rectum* 1997; **40**: 798-801.
  17. Kitamura A, Kanagawa T, Yamada S, Kawai T: Effective chemotherapy for abdominal desmoid tumor in a patient with Gardner's syndrome: Report of a case. *Dis Colon Rectum* 1991; **34**:822-826.
  18. Seiter K, Kemeny N: Successful treatment of a desmoid tumor with doxorubicin. *Cancer* 1993; **71**:2242-2244.
  19. Kiel KD, Suit HD: Radiation therapy in the treatment of aggressive fibromatoses (desmoid tumors). *Cancer* 1984; **54**:2051-2055.