Mesenteric Desmoid Tumor in Gardner's Syndrome Treated by Sulindac

PAUL BELLIVEAU, M.D., A. M. GRAHAM, M.D.

Belliveau P, Graham AM. Mesenteric desmoid tumor in Gardner's syndrome treated by sulindac. Dis Colon Rectum 1984;27:53-54.

Mesenteric desmoid tumors are a recognized sequela of colectomy for polyposis coli of Gardner's type. Relentless growth and recurrence carry a poor prognosis. Recently, nonsteroidal anti-inflammatory drugs have been used to halt the growth of these tumors, presumably by interfering with prostaglandin metabolism. A 36-year-old man presented with small-bowel obstruction secondary to a large, diffuse mesenteric desmoid six years following colectomy and ileoproctostomy. Laparotomy revealed it to be unresectable. Postoperatively, he was started on sulindac (Clinoril®) 100 mg twice a day. His obstruction resolved, and he remains well at 11 months. A CT scan shows diminution in the size of the tumor. Nonsteroidal anti-inflammatory agents may be an alternative to chemotherapy and radiotherapy in treating mesenteric desmoids. [Key words: Familial polyposis coli; Gardner's syndrome; Mesenteric desmoid; Therapy]

THE TREATMENT OF DESMOID TUMORS of the abdomen in patients with familial polyposis has been disappointing because of the high rate of recurrence (27 to 57 per cent)[1] and the inability of the surgeon to apply the principle of radical excision to tumors affecting the mesentery extensively. These nonencapsulated histologically benign tumors proliferate by invasion and produce intractable obstruction from pressure on adjacent structures. Their incidence is approximately 4 per cent in all patients with Gardner's syndrome. In a collected series of 89 desmoids, 73 developed following colectomy for familial polyposis coli, usually within two years, and 42 were mesenteric.[2] There is a general feeling that these tumors arise as a result of the trauma of the original surgery; there are, however, reported cases of spontaneous appearance of these tumors.[3] Radiotherapy has had some success with extra-abdominal desmoids,[4] and it is unclear whether reduced doses used against abdominal lesions would have an effect. Chemotherapy similarly has had sporadic success.[5]

Read at the meeting of the American Society of Colon and Rectal Surgeons, Boston, Massachusetts, June 5 to 9, 1983.

Address reprint requests to Dr. Belliveau: Department of Surgery, St.-Mary's Hospital, 3830 Lacombe Avenue, Montreal, Quebec, Canada H3T 1M5

From the Department of Surgery, St.-Mary's Hospital, McGill University, Montreal, Quebec, Canada

Waddell postulated that inhibition of prostaglandin synthesis may have a role in the control of tumor growth, and he used nonsteroidal anti-inflammatory drugs to obtain tumor regression in six of seven patients with desmoids of the chest (2), abdominal wall (2), or small-bowel mesentery (3).[6,7] This form of therapy was used in our patient and is the basis of this report.

Report of a Case

A 36-year-old man presented to the emergency department, complaining of crampy abdominal pain of four hours' duration. He denied vomiting and had had a semi-formed bowel movement earlier that day but none since. He recalled an episode of pain and diarrhea six months earlier, while vacationing in Mexico, and had noticed a mass in his abdomen but failed to inform his doctor. Past medical history included total abdominal colectomy and ileoproctostomy six years prior for Gardner's syndrome.

On examination, he was well hydrated and afebrile. He had a sebaceous cyst on the forehead. Abdominal examination revealed high-pitched bowel sounds and moderate distention. Abdominal series were consistent with small-bowel obstruction. Following initial nasogastric decompression, a large mass in the right side of the abdomen, deep to the musculature, nontender, and measuring 17 by 15 cm, became palpable. Sigmoidoscopy showed 12 small rectal polyps. Hemoglobin was 18.9 gm, and the white blood count was normal. Abdominal ultrasound revealed a solid mass not attached to the abdominal wall, and an intravenous pyelogram showed compression of the right ureter. A CT scan showed a large irregular mass, extending from just behind the rectus muscle to just anterior to the psoas, with small-bowel loops involved in it. The superior mesentenic artery (SMA) arteriogram demonstrated the ileocolic artery stretched over an avascular area, corresponding to the palpable mass.

His bowel obstruction did not completely resolve and he was started on total parenteral nutrition (TPN). At laparotomy, an enormous unresectable tumor was found, involving the entire small-bowel mesentery. It extended from the diaphragm on the left in the retrogastric area to the right side of the pelvis. Numerous loops of small intestine were within it and stretched over the tumor. Following some mobilization of the mass, it was noted that the right ureter and the vena cava were involved. Biopsy revealed a benign desmoid tumor. A 2-cm desmoid in the previous scar was excised. He was continued on nasogastric suction and TPN, and after two weeks his obstruction had improved so that he could tolerate liquids. The patient was started on sulindac, 100 mg orally twice a day, and he showed prompt improvement. He was maintained on a blenderized diet for two months and gradually progressed to a normal diet. The palpable mass clinically is smaller (14 by 14 cm), and a repeat CT scan

shows slight diminution of the tumor. He is active at work and maintains his normal weight at ten months. The dose of sulindac was increased to 150 mg twice a day for easier administration.

Discussion

Approximately 64 cases of mesenteric desmoids have been reported in the English medical literature. The first major review was in 1970 by McAdam and Goligher.[2] Their comment that "the principle of wide excision is hard to apply to mesenteric desmoids" was repeated in most of the case reports. Since resection is of limited value due to the advanced stage of many mesenteric desmoids, trials of bypass, interstitial radiation therapy, and chemotherapy have been suggested to prevent progression of the tumors.[8] Long-term parenteral nutrition carries the risks of catheter sepsis and is not an ideal solution. Our case demonstrates that by the time a mesentric desmoid is detected it has often grown to an enormous size and has involved itself about the mesenteric vessels, with many loops of bowel wrapped around or encased by the tumor.

The treatment of these patients can only begin after a thorough radiologic work-up, including barium studies, CT scanning, and arteriography. The best treatment is still surgical excision, but the diffuseness of the tumor, as well as its location around vital structures, often precludes this. Even after excision, the recurrence rate has been estimated at 27 to 57 per cent.[1]

Radiotherapy has been advocated, but its effectiveness in treating mesenteric desmoids has not been proven.[4] Various chemotherapeutic agents have been tried, with only scattered success.[5] Other treatment regimens have been sought, and one of these involved inhibition of cyclic adenosine monophosphate phosphodiesterase. Drugs such as theophylline, chlorothiazide, testolactone, and ascorbic acid have been used, based on extensive literature that advocates the use of cyclic AMP manipulation in the inhibition of tumor cells. In 1975, Waddell reported shrinkage of a pelvic desmoid with these agents.[9] However, Harvey *et al.* reported failure of this therapy in two cases.[8]

The next approach to medical therapy has been based on prostaglandin synthesis inhibition. *In vivo* studies demonstrated resolution of rodent fibrosarcomas by prostaglandin manipulation.[10] The mechanism is unclear, but it is felt that the prostaglandin effect on the immune system is inhibitory and that by decreasing its synthesis the immune response can be enhanced by increased numbers of T-cells and killer cells. Nonsteroidal anti-inflammatory drugs, such as indomethicin and sulindac, are known inhibitors of prostaglandin synthesis and have found clinical use in some patients with desmoids. In addition, ornithine decarboxylase, an enzyme associated with tumor proliferation, has been shown to be inhibited by indomethicin.[6]

There has been sporadic success in the use of tamoxifen in treating desmoids in females. The effect of estrogen blockade is felt to restrict RNA synthesis and alter transcription of genes involved in tumor growth. Tamoxifen inhibits prostaglandin synthesis. These agents, alone or in combination, may be of great benefit to those patients who have unresectable desmoid tumors.

Mesentric desmoid tumors are often a very serious and distressing complication in young patients with Gardner's syndrome in whom prophylactic colectomy has been carried out to prevent carcinoma from developing. Although rare, these abdominal masses must be diagnosed as such and not assumed to be recurrent malignancy. After a complete assessment by intravenous pyelography, arteriography, and CT scan, they should be explored with the intention of resection. If this is not possible, a trial of sulindac, with the addition of tamoxifen in females, is justified, with CT scan follow-up.

References

1. Naylor EW, Lebenthal E. Gardner's syndrome: recent developments in research and management. Dig Dis Sci 1980;25:945–59.
2. McAdam NA, Goligher JC. The occurrence of desmoids in patients with familial polyposis coli. Br J Surg 1970;57:618–31.
3. Richards RD, Rogers SW, Gardner EJ. Spontaneous mesenteric fibromatosis in Gardner's syndrome. Cancer 1981;47:597–601.
4. Wara WM, Phillips TL, Hill DR, et al. Desmoid tumors: treatment and prognosis. Radiology 1977;124:225–6.
5. Karakousis CP, Berjian RA, Lopez R, Ras U. Mesenteric fibromatosis in Gardner's syndrome. Arch Surg 1978;113:998–1000.
6. Waddell WR, Gerner RE, Reich MP. Nonsteroid anti-inflammatory drugs and tamoxifen for desmoid tumors and carcinoma of the stomach. J Surg Oncol 1983;22:197–211.
7. Waddell WR, Gerner RE. Indomethicin and ascorbate inhibited desmoid tumors. J Surg Oncol 1980;15:85–90.
8. Harvey JC, Quan SH, Fortner JG. Gardner's syndrome complicated by mesenteric desmoid tumors. Surgery 1979;85:475–7.
9. Waddell WR. Treatment of intra-abdominal and abdominal wall desmoid tumors with drugs that affect the metabolism of cyclic 3′5′ adenosive monophosphate. Surgery 1975;81:299–302.
10. Hial V, Horakova A, Shaff RE. Alteration of tumor growth by aspirin and indomethicin: studies with two transplantable tumors in mouse. Eur J Pharmacol 1976;37:367–76.