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CASE REPORT | INFLAMMATORY BOWEL DISEASE

Mesenteric Fibromatosis in Crohn's Disease as a Potential Effect of Adalimumab

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Abstract

A 36-year-old woman with no medical or surgical history was evaluated for weight loss. Abdominal computed tomography (CT) showed signs of Crohn's disease, which was later confirmed endoscopically. She was started on tumor necrosis factor-α (TNF-α) inhibitor therapy. Nine months after treatment, she experienced additional weight loss and a 7 x 8 x 8-cm mass on repeat CT. Biopsy revealed retroperitoneal fibromatosis, so TNF-α was continued. Repeat CT showed an enlarged mass. TNF-α therapy had a suspected role in mass growth, therapy was discontinued, and the mass surgically resected. One year after resection, she has regained weight with no recurrence of the mesenteric fibromatosis.

Introduction

Desmoid tumor (DT), also referred to as aggressive fibromatosis, is a monoclonal proliferation of myofibroblasts that extensively infiltrate adjacent muscle tissue, tendons, and musculoskeletal structures.[1,2] The pathogenesis of these tumors is not fully understood, but multiple mechanisms have been proposed. The development of DT has been most commonly associated with mutations in the ß-catenin gene, given its high prevalence rate in familial adenomatous polyposis (FAP). DT affect about 15% of patients with FAP-associated with Gardner's syndrome, which is caused by adenomatous polyposis coli gene (5q21-22) mutations.[3,4]

Despite not commonly metastasizing, their morbidity and mortality are often due to a functional disorder of the extensively infiltrated structures. When associated with FAP, DT are usually intra-abdominal, more aggressive, often surgically unresectable, and carry an increased mortality of about 11%.[5] The primary treatment is surgical resection, though recurrence is possible, especially when associated with FAP in which radiation and, less commonly, chemotherapy are used.[6,7]

Case Report

A 36-year-old woman with no prior medical or surgical history presented with continued unexplained weight loss and nonspecific abdominal pain and anorexia. Abdominal computed tomography (CT) showed no distinct masses but did show extensive segmental small bowel wall thickening, suggestive of Crohn's disease (CD), which was confirmed by endoscopy. Two weeks after initial upper endoscopy, intrauterine levonorgestrel, a synthetic progestin, was inserted to decrease menorrhagia, and remained implanted throughout her care.

Systemic glucocorticoids were initially started, but were poorly tolerated. She was started on adalimumab and tolerated treatment for 9 months, when she presented with an additional 5-kg weight loss. Repeat CT showed a 7 x 8 x 8-cm enhancing, lobulated mass to left of the abdomen and mesenteric adenopathy. A PET/CT showed a possible

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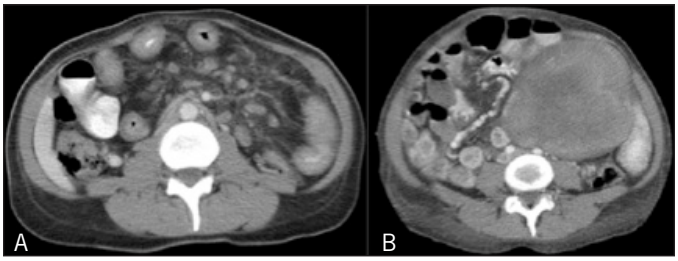

Figure 1. Abdominal CT showing (A) extensive segmental small bowel wall thickening suggestive of Crohn's disease and centrally mesenteric adenopathy, but no distinct mass, and (B) a 12.1 x 10.8 cm enlarging homogeneous, solid mass left of the midline.

necrotic center. A CT-guided biopsy revealed retroperitoneal fibromatosis. Given the benefits of biologic therapy for a patient with symptomatic CD and lack of evidence of desmoid tumors associated with adalimumab, TNF-α inhibitor therapy was continued.

Several months later, surveillance abdominal CT showed the mass had enlarged (Figure 1). She underwent an exploratory laparotomy, during which 107 cm of segmental small bowel was resected with en bloc tumor resection, and a 1° side-to-side functional end-to-end jejunal anastomosis was completed (Figure 2). Histology suggested the tumor originated from the small bowel wall rather than via infiltrative process (Figure 3). Margins were negative, so adjuvant radiotherapy was reserved for potential recurrence. One year after resection, she is off of biologic therapy, has regained her weight, and there is no evidence of mass recurrence. She will be monitored for recurrence with annual CT scans.

Discussion

Development of mesenteric fibromatosis (MF) has been associated with CD in patients with a history of FAP, after any abdominal surgery,[8] and in a hyper-estrogenemic state.[9-11] DTs can develop sporadically throughout the body and abdominal wall, and can be site-specific if induced by trauma. It is essential to exclude possible modifiable triggers. She was in a low-estrogen state due to intrauterine (IU) synthetic progestin therapy. Her IU progestin therapy remained before and continued after en-bloc resection more than 1 year. Given the lack of recurrence based on radiography, it is unlikely that progesterone played a role in this case. The relation of progesterone with DT and respective treatment options remains trivial and inconclusive.[10]

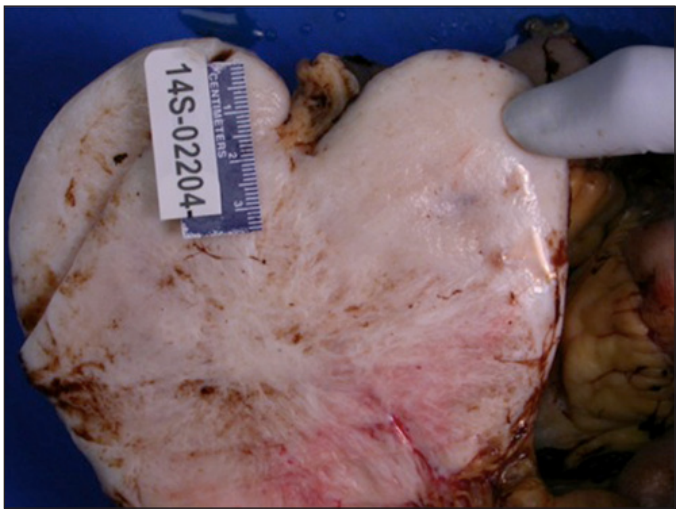

Figure 2. Gross specimen of the 14 x 13 x 11-cm mesenteric desmoid tumor originating from the proximal jejunum, adherent unifocally to the small bowel.

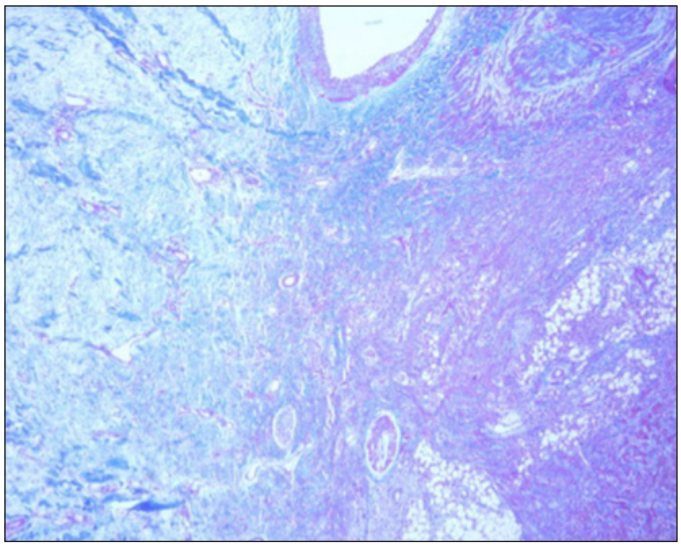

Figure 3. Trichrome stain showing the desmoid tumor (left) and the muscularis layer of the small bowel (right) with a regular, non-disrupted interface.

The literature relating MF to TNF-α therapy is limited. A meta-analysis showed a 0.36% increased incidence of cancer events, about 4.5 times higher than that of the control group within 6 months of treatment with adalimumab.[12] Another meta-analysis of rheumatoid arthritis patients initiated on adalimumab found there was a dose-dependent increased incidence of solid malignancies as early as 6–12 months.[13] Differences in study populations, study practices, and data reporting create challenges in conclusively determining the relationship of TNF-α therapy and malignancy in CD. Despite the low incidence of new neoplastic events, our case underscores that CD patients taking TNF-α therapy should be closely monitored, even in the absence of risk factors for malignancy.

Disclosures

Author contributions: All authors contributed equally to the creation of this manuscript. A. Abdelqader is the article guarantor.

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