

CASE REPORT

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# Mesenteric desmoid fibromatosis entrapping metastatic urothelial carcinoma: a unique collision tumor or fibromatosis-like variant?

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## Abstract

A collision tumor is a neoplastic lesion comprised of two or more distinct cell populations with distinct borders. Desmoid fibromatosis (DF) is a rare musculoaponeurotic tissue tumor that grows deep in the connective tissue and shows locally aggressive behavior. Only two cases of collision tumors with desmoid fibromatosis are reported in the English literature, albeit papillary thyroid carcinoma with desmoid fibromatosis-like stroma is regarded as a variant rather than a collision tumor. We present a unique case of collision tumor with desmoid fibromatosis surrounding intra-abdominal metastasis from urothelial carcinoma. A 65-year-old white male with history of bladder and left renal pelvis high-grade papillary urothelial carcinoma status post-nephrectomy was found to have a small bowel obstruction due to a soft tissue mass. Histology of the mass showed multiple matted lymph nodes with metastatic urothelial carcinoma admixed with a proliferation of spindle cells positive for nuclear beta-catenin, consistent with desmoid fibromatosis. While the prior surgical site likely acted as a nidus for development of desmoid fibromatosis, we also hypothesize that a dysregulation of beta-catenin signaling pathways within the cancer cells might have attributed to the spindle cell proliferation in the stroma surrounding the tumor. Our case emphasized the importance of clinical suspicion of desmoid fibromatosis in patients with metastatic cancer, requiring a prompt diagnosis and treatment to decrease the risk of complications and local recurrence.

**Keywords:** Collision tumor, Desmoid fibromatosis, Urothelial carcinoma, Beta-catenin, Soft tissue

## Introduction

Desmoid fibromatosis (DF) is a rare musculoaponeurotic tissue tumor that grows deep in the connective tissue and shows locally aggressive behavior. It accounts for approximately 0.03% of all neoplasms (Sakorafas *et al.* 2007), and its incidence is between 2 and 4 per million (Nieuwenhuis *et al.* 2011). This tumor is more common in females, and cases have been described in subjects between 15

and 60 years of age, with a prevalence between 30 and 40 years (Penel *et al.* 2016). By definition, DF lacks metastatic capacity, but it shows a high rate of recurrence (Gronchi *et al.* 2014).

Most DFs are sporadic, but they may also be hereditary (familial DF). In most cases, familial DF develops in subjects with familial adenomatous polyposis, who have 1000 times increased risk of developing DF (Gurbuz *et al.* 1994; Desmoid Tumor Working Group 2020). The most common location for sporadic DF is the abdominal cavity (Fiore *et al.* 2016), while in familial DFs, the tumor commonly develops at a prior surgical site (Koskenvuo *et al.* 2017).

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Multiple risk factors have been hypothesized in DF development, including previous surgeries, pregnancies (especially with cesarean section), traumas, inflammatory bowel disease, and oral contraceptives. However, the exact pathophysiology is still not completely understood (Martinez Trufero et al. 2017).

We present a unique case of desmoid fibromatosis surrounding intra-abdominal metastasis from urothelial carcinoma. After resection of the mass, the histology and immunohistochemistry confirmed the diagnosis. This is the first reported case of a DF entrapping a urothelial carcinoma in the English literature to the best of our knowledge.

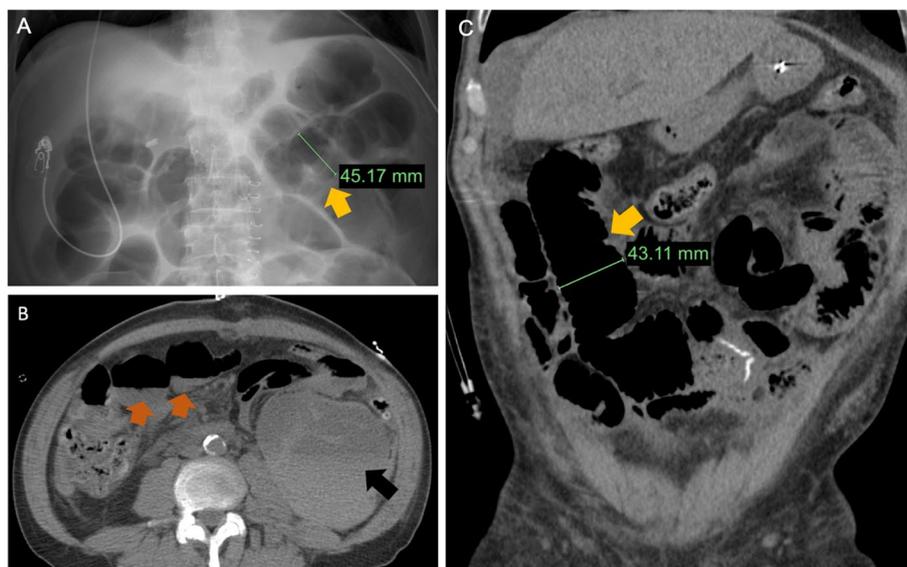
### Case report

The case regards a 65-year-old white male with a past medical history of anxiety, hypertension, hypothyroidism, left renal pelvis high-grade papillary urothelial carcinoma status post-nephrectomy, and diffuse large B-cell lymphoma, who presented to the Emergency Department with abdominal pain, severe nausea, and emesis. The primary renal pelvis urothelial carcinoma was originally stage as pT1N0. Additionally, the patient had a history of high grade urothelial carcinoma of the bladder treated with transurethral resection and BCG. He previously received Rituximab CHOP chemotherapy for his lymphoma. A year and a half prior to admission the patient was started on Gemzar/Cisplatin, and Keytruda for presumed metastatic bladder carcinoma. Lab analyses were

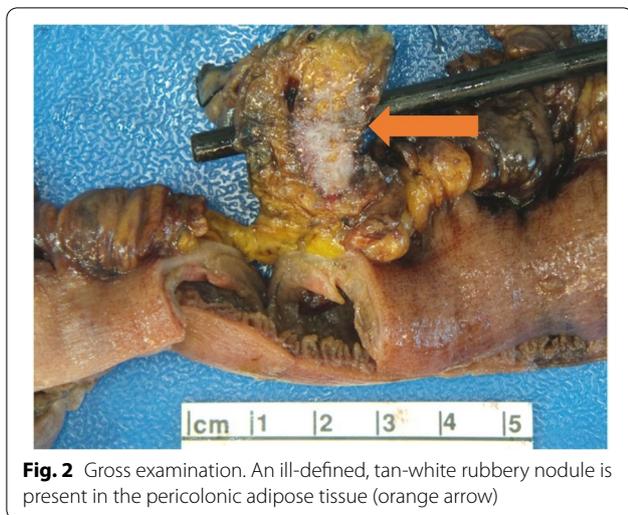
notable for leukocytosis of 13.1, elevated creatinine of 1.94, and lactate of 0.8. A Computed Tomography (CT) scan showed evidence of small bowel obstruction due to left abdominal adhesions from a previous nephrectomy. Imaging also revealed a soft tissue mass suspicious for malignancy in the left renal fossa at the site of obstruction (Fig. 1).

The patient was scheduled for an exploratory laparotomy that revealed a small bowel obstruction due to adhesions in the left renal fossa. He then underwent lysis of adhesions and partial small bowel resection. The resected segment of small bowel was sent to the pathology department for evaluation. At the gross examination, the specimen consisted of a 42.0 × 2.0 cm portion of small bowel with a predominantly pink-gray smooth surface and focal area of dark serosal discoloration and serosal adhesions. On opening, the mucosa showed a focal area of hemorrhage and mucosal flattening, consistent with obstruction. In the adipose tissue surrounding the bowel, 6.0 cm from the closest bowel resection margin, a 3.5 × 1.4 × 1.1 cm tan-white, ill-defined, rubbery mass was detected, grossly involving the pericolonic adipose tissue but not the bowel wall (Fig. 2).

Histology of the mass showed multiple matted lymph nodes with metastatic urothelial carcinoma (Fig. 3A). The carcinoma was positive for CK7, CK20, cytokeratin ae1/ae3, GATA-3 (Fig. 3B), and membranous B-catenin (Fig. 3C). Moreover, a proliferation of spindle cells positive for nuclear beta-catenin was observed surrounding



**Fig. 1** Initial imaging with abdominal plain film demonstrated dilated loops of bowel measuring over 4 cm in diameter representing ileus versus an obstruction (A). This was confirmed on cross-sectional computed tomography imaging without contrast. On axial (B) and coronal (C) images showing dilated loops of small bowel measuring up to 4.3 cm (filled yellow arrows) with multilevel differential air fluid levels (filled orange arrows) consistent with small bowel obstruction (SBO). A left abdominal soft tissue mass lesion was observed in the left renal fossa. (filled black arrow)



**Fig. 2** Gross examination. An ill-defined, tan-white rubbery nodule is present in the pericolonic adipose tissue (orange arrow)

the foci of metastatic urothelial carcinoma (Fig. 3D-F). The findings were consistent with desmoid fibromatosis (Fig. 3).

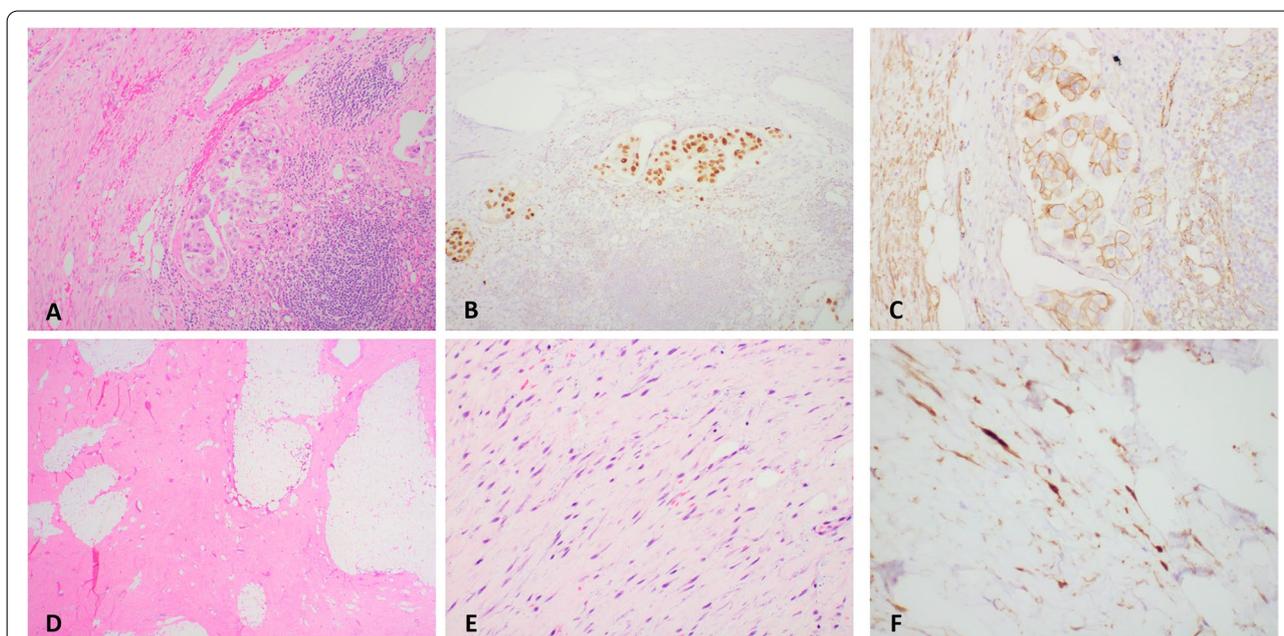
The patient was discharged in good condition approximately 1 week following surgery. At discharge, the patient was hemodynamically stable and tolerated diet, denied any nausea or vomiting, was voiding and continued to have bowel movements.

### Discussion

DF is a slow-growing tumor that may remain silent for a long time and even undergo spontaneous remission. This entity is usually asymptomatic or may cause nonspecific symptoms due to the mass effect on the adjacent structures (compression or obstruction). Due to its clinical and radiological features, DF can mimic a malignancy within the organ where it arises. Intra-abdominal DFs generally involve the mesentery or celiac axis, resulting in obstruction, perforation, or bleeding.

Imaging studies contribute to the diagnosis. CT scan shows typically a deep soft tissue mass that is better characterized by Magnetic Resonance Imaging (MRI). However, the final diagnosis requires surgical excision and microscopic examination. Surgery is the primary treatment of intraabdominal DFs and allows a long-term disease-free period.

Histologically, DF demonstrates a fascicular proliferation of bland elongated spindle cells resembling myofibroblasts in a collagenous stroma and vascular network (Muller et al. 1996). Atypia or increased mitotic activity are generally not present. Immunohistochemistry is commonly positive for nuclear beta-catenin, which is helpful to confirm DF and differentiate it from other benign and malignant fibroblastic and myofibroblastic lesion (Bhattacharya et al. 2005). The significance of beta-catenin in the diagnosis of DF lies in the molecular pathogenesis of the tumor, which is related to the APC gene and



**Fig. 3** Microscopic examination of the mesenteric nodule. (A) H&E, 100X) Islets of metastatic urothelial carcinoma are seen within the lymph node. The tumor cells are positive for GATA-3 (B) and membranous beta-catenin (C). A spindle cells stroma proliferation surrounding the foci of metastatic urothelial carcinoma (D) H&E, 20X; E) H&E, 200), with positive nuclear beta-catenin stain (F)

the *Wnt/B-catenin* cascade. The *APC* gene regulates the phosphorylation and proteasomal degradation of beta-catenin. The *Wnt* pathway normally inhibits APC-dependent phosphorylation, resulting in the activation of beta-catenin.

Beta-catenin is a protein with multiple functions that critically determine fetal cell development and adult cells regenerating processes (Escobar et al. 2012). In physiological conditions, the absence of Wnt keeps beta-catenin at a low level due to proteasomal degradation induced by APC-dependent phosphorylation. When Wnt is activated, beta-catenin increases within the cytoplasm and then translocates into the nucleus. Within the nucleus, it binds the cofactors LEF-1 (lymphocyte enhancer factor-1) and TCF4 (Transcription Factor 4). The complex induces the transcription of tissue-specific target genes. The inhibition of beta-catenin deactivation leads to its accumulation into the cytoplasm and its uncontrolled translocation into the nucleus, representing a significant risk factor for carcinogenesis (Shang et al. 2017). In the setting of familial adenomatous polyposis, desmoid fibromatosis occur from APC inactivation. However, in sporadic desmoid fibromatosis, mutations in APC are not typically seen, and *CTNNB1* (gene for beta-catenin) mutations are more common.

After a review of the English literature, only two cases of collision tumors with desmoid fibromatosis have been reported. The aforementioned cases include a pancreatic mucinous neoplasm and a medullary thyroid carcinoma. A case of collision tumor involving a pancreatic mucinous neoplasm and DF has been described (Ryu et al. 2021). The authors reported the case of a 30-year-old pregnant woman with a mixed solid and cystic mass located in the pancreatic tail. Gross examination revealed two independent masses in the pancreas: one solid and the other cystic. The solid mass demonstrated invasion into the colon and was composed of fibroblastic/myofibroblastic cells arranged in mainly short fascicles in an abundant myxoid matrix consistent with DF. The cystic component was lined by mucinous epithelium with ovarian-like stroma, consistent with a pancreatic mucinous neoplasm. The authors hypothesized that both tumors could have been resulted from hormonal changes related to pregnancy. In another paper, the authors reported a case of medullary thyroid carcinoma embedded in stroma with nuclear beta-catenin expression, suggesting DF (Cho and Oh 2020). Beta-catenin immunostaining showed membranous expression in the epithelial cancer cell nests, and nuclear expression in spindle cells of the stroma. In comparison, papillary thyroid carcinoma with fibromatosis-like stromal component is regarded as a variant of papillary thyroid carcinoma, and not a collision tumor (Wong et al. 2019). This raises the question of

whether the current case should be regarded as a collision tumor, and rather a variant of urothelial carcinoma with fibromatosis-like stroma.

In the present case, DF was detected in the context of small bowel obstruction in a patient with history of urothelial carcinoma and nephrectomy. The soft tissue mass involved the adipose tissue surrounding the small bowel in the left renal fossa, site of the remote nephrectomy performed approximately 2 years and 6 months earlier. A previous imaging study performed before the nephrectomy did not reveal any mesenteric mass.

We observed an unusual DF involving a mesenteric metastasis from urothelial carcinoma. The reason why the DF arose specifically surrounding the metastatic urothelial carcinoma is not clear but is likely related to the prior surgery. However, another possible explanation is that both tumors may share a *Wnt/β-catenin* molecular aberrancy. It has been observed that mutations in the regulatory components of the *Wnt/β-catenin* pathway are present in approximately one third of urothelial carcinomas (Ahmad 2015; Garg and Maurya 2019; Majid et al. 2012).

It is hypothesized that cancer cells may affect the microenvironment of surrounding normal tissues. As a result, the local non-tumor cells can also develop mutations due to chemical stimuli from the tumor (hypoxia and acidosis) or the release of cytokines and growth factors by the cancer cells. Dysregulation of the signaling pathways within the cancer cells may lead to cell abnormalities and tissue disorganization compared to normal, uninvolved tissue, favoring the spindle cell proliferation in the stroma surrounding the tumor (Zalatnai 2006; Laconi 2007).

Although it cannot be excluded that the DF observed in our case was already present and served as a host to the metastasis from urothelial carcinoma, it is questionable that the local microenvironment surrounding the metastatic urothelial carcinoma increased the likelihood of formation of a desmoid tumor.

## Conclusions

The diagnosis of DFs of the small bowel may be challenging. Even if DFs do not metastasize, they are locally aggressive and may lead to severe and potentially life-threatening complications. Although somewhat rare, DFs should always be included in the differential diagnosis of abdominal soft tissue masses. Our case emphasized the importance of clinical suspicion of this relatively rare entity in patients with metastatic cancer, requiring a prompt diagnosis and treatment to decrease the risk of complications and local recurrence. The question of whether this represents a true collision tumor or unique variant of urothelial carcinoma will require additional studies.

**Abbreviations**

DF: Desmoid fibromatosis; CT: Computed tomography; MRI: Magnetic resonance imaging.

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**Authors' contributions**

Lorenzo Gitto and Daniel J. Zaccarini conceived the paper, wrote the manuscript, and supervised the project. Thomas VanderMeer performed the surgery and reviewed the clinical history. David Lubin added the radiology findings. All authors collectively proofread the manuscript and approved it for publication.

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**Declarations****Ethics approval and consent to participate**

Ethical approval not required. SUNY Upstate IRB (Institutional Review Board) does not require review of case reports that do not meet the definition of human subject research. Images reported in this paper have been reviewed and approved by the Educational Communications department of SUNY Upstate. The investigation was conducted in accordance with the Declaration of Helsinki of 1975.

**Consent for publication**

Not applicable.

**Competing interests**

The authors have no competing interests.

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