Resolving The Diagnostic and Management Dilemma: A Case of Giant Sporadic Mesenteric Fibromatosis And Review Of The Literature

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Abstract

Mesenteric fibromatosis (MF) is a benign intra-abdominal mesenchymal tumour and its radiological features are nonspecific leading to frequent misdiagnosis and current literature for management consensus is lacking. We describe a case and review the literature.

A 26-year-old gentleman presented with symptomatic abdominal distension and an epigastric mass to our institution. Imaging showed a large heterogenous mass arising from the root of the mesentery. En bloc resection including right hemicolectomy and small bowel resection was performed for proper tumour clearance. Histology revealed mesenteric fibromatosis with clear margins. The patient has been disease free for 18 months.

Sporadic giant MF is a rare clinical entity that presents as both a difficult diagnostic and management issue. Despite the use of imaging and pre-operative biopsy to improve diagnostic rates, treatment is complex and may result in radical resections associated with significant morbidity. Surgery with disease-free resection margins provides the best possibility of cure with no recurrence in patients who are symptomatic or have complicated disease that are deemed resectable.

KEYWORDS: Mesenteric Fibromatosis, Desmoid Tumor
Introduction

Mesenteric Fibromatosis (MF) is a benign, intra-abdominal mesenchymal tumour comprising spindle shaped and myofibroblast-like cells. Although non-metastatic, it is locally invasive and prone to recurrence. (1–3) The radiologic features of MF are non-specific, and coupled with its location in the mesentery, results in frequent misdiagnosis. (4) This may result in inappropriate therapeutic decisions. Its large size, local growth and invasion to surrounding intra-abdominal structures further add to its clinical complexity. We describe the case of a 26-year-old man presenting with abdominal distension and ureteric obstruction secondary to giant MF of the small bowel mesentery, who was treated with surgery. In addition, we review the literature for the diagnostic and therapeutic dilemma surrounding MF and describe this rare clinical entity of giant, sporadic MF.

Case Study

A 26-year-old gentleman presented to the emergency department with a 1-month history of abdominal distension. There was no history of nausea, vomiting, change in bowel habits, weight loss or loss of appetite. No previous abdominal surgery or trauma was noted. On examination, there was a hard, non-tender epigastric mass measuring 20 x 10cm. (Figure 1) The mass was non-pulsatile and moved with respiration. No peripheral lymphadenopathy was found. Laboratory examinations were not significant. Computed Tomography (CT) of the abdomen and pelvis revealed a well-defined, heterogeneously enhancing soft-tissue mass measuring 23cm x 19cm x 11cm in the root of the mesentery. The mass was seen splaying bowel loops and mesenteric vessels. Fortunately, patency of the superior mesenteric artery and gastroduodenal artery was preserved. Direct mass effect on the right ureter resulted in mild right hydronephrosis. There was no intra-abdominal lymphadenopathy or evidence of bowel obstruction. (Figure 2)

Surgical Technique

In view of the clinical suspicion of a desmoid tumor, the patient was counseled for and underwent an exploratory laparotomy and resection of the intra-abdominal tumor. A double-J stent was inserted to decompress the enlarged right ureter prior to the exploratory laparotomy. Intraoperative findings noted a large mesenteric mass measuring 25cm x 18.5cm x 16cm and weighed 3.8kg. (Figure 3) The mass was found originating from the junction of the ileocolic vessels from the superior
mesenteric vessels and was closely adherent to the middle colic vessels. It was also adherent to terminal ileum, caecum and ascending colon. (Figure 4) Bowel reconstruction was a functional end-to-end ileocolic anastomosis after 100 cm of small bowel resection and right hemicolectomy was performed for appropriate tumor clearance. The patient’s post-operative recovery was uneventful and was discharged well on post-operative day 10.

Pathology

Histological examination revealed interlacing bundles of spindle cells in a mixed collagenous stroma. Tumour cells were hypochromatic with relatively few mitotic figures observed. Immunohistochemistry showed positive peri-nuclear β-Catenin granules but negative nuclear expression. Tumour cells were immunonegative for Smooth Muscle Actin, Desmin, CD34, CD99, CD117, S-100, DOG-1 and Epithelial Membrane Antigen. In the context of the given histology, the immunohistochemical findings were suggestive of mesenteric fibromatosis, confirming the diagnosis. The patient subsequently underwent gastroscopy and colonoscopy performed which did not show any intestinal polyposis. Subsequent imaging at 18 months post-resection showed no evidence of tumor recurrence.

Discussion

Although desmoid tumours may be found extra-abdominally in the soft tissues of the limbs, mediastinum, head and neck, they are predominantly found intra-abdominally. Intra-abdominal desmoids tumors are located within the mesentery, retroperitoneum, pelvis and abdominal wall. These are also known as aggressive/deep fibromatoses. Intra-abdominal desmoids tumors account for 28-69% of all desmoids (2) and small bowel mesentery is the commonest site of occurrence. MF has an incidence of 2-4 per million persons per year. (1) This accounts for a mere 0.03% of all neoplasms, and 3% of mesenchymal tumours. (1) The literature suggests a slight female preponderance in MF. However, a clear gender association is only seen in desmoid tumours occurring in the abdominal wall. (4) Proposed risk factors for MF include prior abdominal surgery, abdominal trauma, and hyper-oestrogenaemic states including pregnancy and oral contraceptive use. (2) Although a possible association with Crohn’s disease has been reported, it has only been limited to one case report in literature thus far. (3) Most desmoid tumours are sporadic, with 13-20% related to Gardner’s syndrome and Familial Adenomatous Polyposis (FAP). (2) Hence, given this genetic
association, all patients with MF should have gastroscopy and colonoscopy to identify polyposis, which was undertaken in our patient who had no other documented risk factor of MF.

Of all deep fibromatoses, MF may have a more symptomatic clinical course due to its location in the mesentery, proximity to surrounding structures and local aggressiveness. MF may present with one of a myriad of symptoms, such as abdominal distension, pain, nausea or secondary to local complications including intestinal obstruction, perforation and haemorrhage. Rare presentations include ureteric obstruction, irreducible hernias and fistulae. Huss et al conducted a clinico-histopathological study on 56 MF tumours and reported median tumour length was 9.4cm (range 2-30 cm). Our patient has a tumour length of 25cm, and based on tumour volume and gross weight of 3.8kg, represents one of the largest reported in the literature, thus belonging to a clinical entity described as giant MF.

MF is especially challenging to diagnose due to its bulky, solid appearance, localised origin in the mesentery and invasion of surrounding tissues on imaging, akin to Gastro-Intestinal Stromal Tumours (GIST) and spindle cell sarcomas. In contrast, extra-abdominal or abdominal wall type fibromatosis tend to spread in 2-dimensional fibrous planes. This peculiar difference in tumour behaviour in MF contributes to radiological misdiagnosis. Huss et al reports a 68% misdiagnosis rate for MF in his series, with the majority misdiagnosed as GIST. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are the main imaging modalities used to aid diagnosis, assess pre-operative mass characteristics and relation to surrounding structures. CT features of MF include a soft tissue attenuation pattern that may be homogenous or heterogeneous, depending on the relative amounts of collagenous and myxoid stroma comprising the tumour, respectively. MRI, with its excellent soft tissue definition, shows up MF as a heterogeneous intermediate on T1-weighted images and high signal intensities on T2-weighted images. T2-weighted imaging may also prognosticate the aggressiveness of MF; stronger signal intensity is associated with rapid tumour growth. Additionally, there has been reported usage of Contrast Enhanced Ultrasound guided core-biopsy (CEUS), Video-assisted laparoscopic biopsy with mutational analysis and immunohistochemistry of tissue samples thereafter to obtain pre-operatively diagnosis of MF over other differentials, especially GIST and retroperitoneal sarcomas.

The histological diagnosis of MF presents a dilemma due to its similarities to spindle cell neoplasms, dedifferentiated liposarcomas, GIST, and given its rarity, the lack of exposure/knowledge in histopathologists. Peculiar microscopic findings suggestive of MF include: proliferation of uniform elongated spindle cells.
cells that infiltrate surrounding tissue, stellate cells with hypochromatic nuclei within a variable collagenous stroma, thin walled dilated vessels, keloid-like collagen deposits and paucicellular perivascular spaces. (4,7,11) Lower mitotic rates and absence of haemorrhage and necrosis are observational differences in distinguishing MF from GIST. (5) In addition to the abovementioned differentials, such histology may be misdiagnosed as sclerosing mesenteritis and keloid-like fibrosis. Immunohistochemistry has become commonplace in aiding diagnosis and differentiation of MF from GIST. 92.7% of all MF’s had $\beta$-Catenin (cadherin-associated protein) nuclear overexpression/staining, a diagnostic feature of MF in the given histology, whereas GIST is classically $\beta$-Catenin negative. Furthermore, immunohistochemical staining for CD34, CD117, smooth muscle actin and desmin are usually negative, features consistent with deep fibromatoses. A high nuclear positivity for $\beta$-Catenin has a specificity of 71% for desmoid type fibromatosis, with few other mesenchymal tumours mimicking this (synovial sarcoma, endometrial stromal sarcoma etc). (12) The CTNNB1 gene codes for the nuclear expression of $\beta$-Catenin. Mutations in exon 3 of CTNNB1 shut down nuclear over-expression of $\beta$-Catenin, thereby accounting for immunonegative MF. (4,10) To account for the remaining 6.3% of MF that are $\beta$-Catenin immunonegative, the corroboration with mutational analysis becomes valuable. In these cases, identification of either mutations in exon 3 of CTNNB1 or presence of the Adenomatous Polyposis Coli (APC) gene (found in FAP) inaugurates the diagnosis.

Lack of a concrete consensus on treatment algorithms for MF is evident, with varying results from limited case reports and case series available in literature. Treatment may involve a trial of watchful waiting, surgical excision, systemic therapy, radiation therapy or a combination of the above. Many authors advocate a radical approach of surgical excision with negative margins. (5,8,12) However, a radical excision results in high morbidity, including bleeding, short gut syndrome and post-operative death. (13) Smith et al documented no survival differences between resected and unresected patients (median duration of follow up of 62 months), noting that some MF tumours have prolonged periods of dormancy or even regression. (13) He attributes this to the biology of desmoids—which grow rapidly in the initial phases followed by stability or regression. Therefore, questioning the role of radical treatment, advocating instead for serial observation or watchful waiting for asymptomatic patients. Nonetheless, surgery is the definitive solution in symptomatic tumours presenting with intolerable symptoms or complications such as intestinal obstruction, perforation or mesenteric ischaemia. (10)

In patients who undergo surgery, a high rate of local recurrence following surgery, as much as 19-77% has been reported. (2) Given the high risk of local
recurrence following excision, adjuvant therapy is on the rise. Studies have shown that the combination of wide excision surgery with adjuvant radiotherapy reduced local recurrence rates. (4,8,12) Garì et al reports a local recurrence of 20-40% with the addition of adjuvant radiotherapy, compared to 40-70% with resection alone. (11)

Due to the anatomical position of MF, some tumours lie in close proximity to vital structures such as the superior mesenteric vessel root, or are excessively adherent to small bowel (necessitating extensive bowel resection to achieve negative margins). These are deemed inoperable, and associated with significant morbidity and mortality if resected as mentioned earlier. Smith et al alludes to cases of severe post-operative mesenteric ischaemia, dependence on total parenteral nutrition and death in these patients. (13) In such cases, and where surgery has failed, systemic therapy may be advocated. A broad range of interventions, including NSAIDs (non-steroidal anti-inflammatory Drugs) (Sulindac), anti-oestrogens (Tamoxifen, Raloxifene), Cytotoxics (Methotrexate, Vinblasticine, Doxorubin) and Tyrosine Kinase Inhibitors (Imatinib) have been reported for inoperable and asymptomatic tumours. However, outcomes have been unpredictable and sporadic. Janinis et al reports at least partial remission in 44% of patients with MF treated with Sulindac (n=9). (14) The rest had stable or progressive disease. From her systematic review of pharmacological treatment in desmoids, she recommends NSAIDs as a 1st line, followed by Tamoxifen and cytotoxics as 2nd and 3rd line respectively. Raloxifene has also been shown to reduce tumour size without significant side effects as well. (12) Imatinib, widely used in GIST therapy has no proven results, while use of Doxorubin and Dacarbacine have achieved at least partial response in 84% of patients with desmoids (n=25 across 4 studies). (15) However, side effects of cytotoxics preclude their use as 1st line agents. Moreover, most of these studies apply to desmoids as a whole, with no specific treatment guideline available at present for MF exclusively. In addition, reports were single-armed with small patient numbers, thereby weakening the argument for medical therapy. (4,8)

**Conclusion**

Giant MF is no doubt a rare clinical entity that presents both as a difficult diagnostic as well as management issue. Despite the use of CT and T2-weighted MRI and the possible adjunctive use of pre-operative biopsy, immunohistochemistry and mutational analyses to improve diagnostic rates of
MF, the treatment complexity of the disease is still a burden for a clinician. These tumors are often symptomatic and local tumor invasion may result in morbid radical resections associated with significant morbidity. Nonetheless, surgery with disease free resection margins provides the only possibility of cure with no recurrence.

References


Figure 1. Mass in relation to anatomical landmarks
**Figure 2.** Computed Tomography (CT) of the Abdomen and Pelvis: Sagittal (A), coronal (B) and axial (C) views

**Figure 3.** Intraoperative picture of the mass
Figure 4. Front and back view of specimen