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Case Report

A Case of Sporadic Desmoid Fibromatosis of the Appendix: A Rare Site of Presentation

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Abstract

***Background*:** Desmoid fibromatosis is a locally aggressive benign fibroblastic soft tissue tumor representing nearly 0.03% of all neoplasms. They can be sporadic or may be associated with Familial Adenomatous Polyposis (FAP). Around 50% of fibromatosis are intrabdominal or arise in the abdominal wall. Rarely, these tumors can arise from the intestinal wall. Appendix and mesoappendix are extremely rare sites of presentation with only 3 reported cases. ***Case Presentation*:** A healthy 43-year-old male presented with abdomen distension. CECT scan showed a well-defined enhancing mass in the lower abdomen attached to the appendix with no surrounding infiltration, fat stranding, or evidence of distant metastasis. A wide resection was performed, and gross examination showed a well-circumscribed mass measuring 8 cm attached to the appendix. Histological examination revealed a well-circumscribed cellular spindle cell neoplasm with focal infiltrative borders. The tumor cells showed nuclear immunoreactivity for Beta-catenin and focally for Desmin, while they were negative for DOG1, CD117, CD34, STAT6, S100 & Pan Cytokeratin. The morphology and immunohistochemistry were compatible with Desmoid fibromatosis. CT scans were negative for recurrence or distant metastases after 8 months of follow-up. ***Conclusion*:** Appendix and mesoappendix desmoid fibromatosis are extremely rare and can present as an abdominal mass or features of acute appendicitis. Gastrointestinal stromal tumor (GIST) is an important differential diagnosis at this site and is crucial to differentiate from fibromatosis for patient management and follow-up. Identifying beta-Catenin (CTNNB1) mutation is a diagnostic criterion to differentiate from other spindle cell tumors, especially on small biopsies. Multi-disciplinary treatment approach is crucial for management.

Keywords: Abdominal Fibromatosis, Desmoid, Appendix, Beta-Catenin, Case Study.

INTRODUCTION

*Desmoid f*ibromatosis is a locally aggressive but non-metastasizing mesenchymal tumour accounting for 0.03% of all soft tissue neoplasms with an incidence of 2 to 4 per million population and with a propensity for local recurrence [4]. 30 to 40% of desmoid fibromatosis present as a mass on the extremities, followed by the abdominal wall (20% cases), retroperitoneum/abdominal cavity (15% cases), and chest wall (15% cases) [11]. Rare sites include the head and neck, paraspinal region, and flank [11]. Intra-abdominal fibromatosis may originate from musculoaponeurotic structures of the body affecting mesentery or retroperitoneum. However, rarely, they can arise from the wall of the gastrointestinal tract [1, 2]. Appendix and mesoappendix are extremely rare sites for fibromatosis and other mesenchymal neoplasms [3]. In these cases, patients usually present with a right iliac fossa mass or with signs and symptoms of acute appendicitis [2, 3].

Microscopy shows sweeping fascicles of spindle cells with a bland appearance surrounded by dense collagenous stroma and infiltration into surrounding soft tissue and fat [4-11]. Lymphoid

aggregates are usually seen at the advancing edge of the lesion [11]. Immunohistochemical studies show positive staining for beta-catenin and smooth muscle actin (SMA). CTNNB1 mutations are reported in 85-90% of cases of sporadic fibromatosis [4]. 5 to 16% of cases of Familial Adenomatous Polyposis (FAP) have associated fibromatosis [4].

Though these tumors have a high incidence of local recurrence, metastatic potential is not identified [4, 5]. CT and MRI scans are helpful in most cases to identify, characterize, and stage the disease [2]. Most cases are treated by surgery; however, complete resection is impossible in some cases which is the most common cause of recurrence [5].

CASE REPORT

A 43-year-old male presented with a 6-month history of abdomen distension. He had no other gastrointestinal symptoms. His appetite was normal and there was no history of weight loss. Colonoscopy showed normal findings. Contrast-enhanced computerised tomographic (CECT) scan showed a 77 x 74 mm well-defined enhancing mass lesion intraperitoneally in the lower abdomen with no surrounding infiltration or fat stranding (Figure 1). The mass showed an area of non-enhancement and represented an area of necrosis. The mass displaced the surrounding bowel loops and was attached to the serosa of the appendix (Figure 1). There was no evidence of distant metastasis. A wide surgical resection was performed.

The gross examination of the specimen showed a well-circumscribed mass measuring 8 x 6.5 x 7.5 cm attached to the appendix. Histological examination showed appendix with a well-circumscribed cellular spindle cell neoplasm with focal infiltrative borders into the meso-appendiceal fibro adipose tissue arranged in intersecting fascicles and bundles in a collagenous stroma (Figure 2). The tumor was present on the inked surface, closely abutting the muscularis layer of the appendix. There were no features of sarcomatous transformation. The appendix was histologically unremarkable. The tumour cells showed immunoreactivity for Beta-catenin and focally for Desmin. The tumour cells were negative for DOG1, CD117, CD34, STAT6, S100 & Pan Cytokeratin (Figure 2). The morphology and immunohistochemistry were compatible with Desmoid fibromatosis.

Somatic genomic profiling was performed using a 550-gene panel (Oncomine Comprehensive Assay Plus). A single nucleotide variant was identified in the hotspot exon 3 region of the CTNNB1 gene (NM_001904.4:c.121A>G p.T41A) (Figure 3). This variant was classified as oncogenic as per the Clingen/CCG/VICC guidelines.

CT scans were negative for recurrence or distant metastases after 8 months of follow-up.

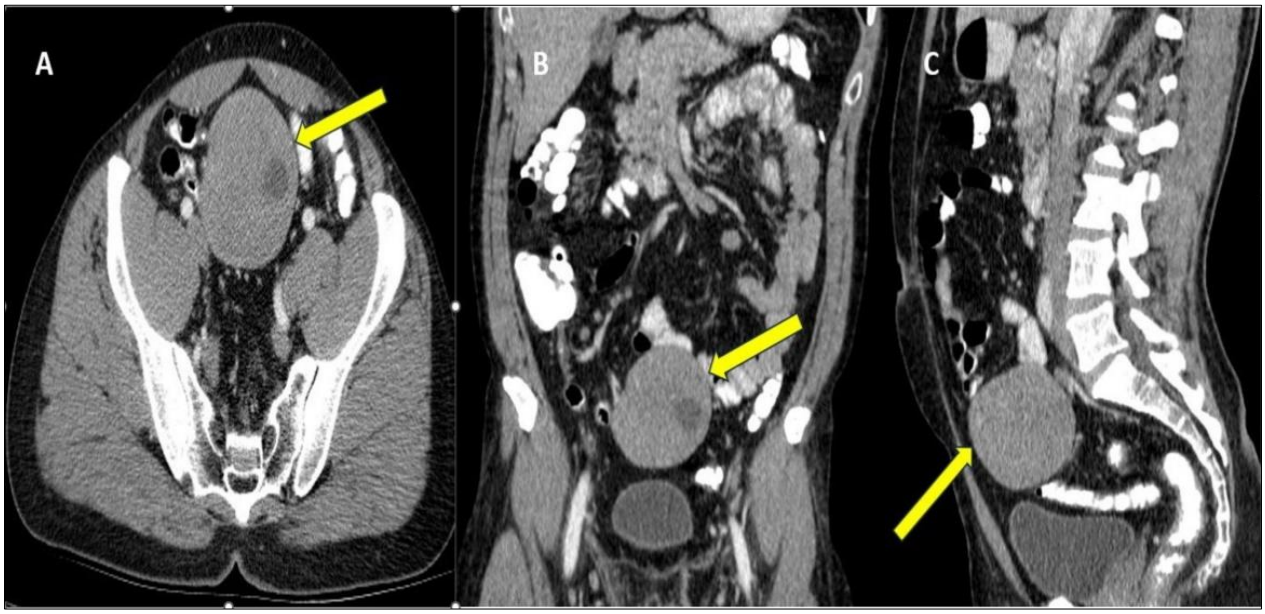

Figure 1: Contrast-enhanced CT scan. Axial (A), coronal (B), and sagittal (C) images show a well-defined enhancing mass lesion noted intraperitoneally in the lower abdomen which is marked with a yellow arrow

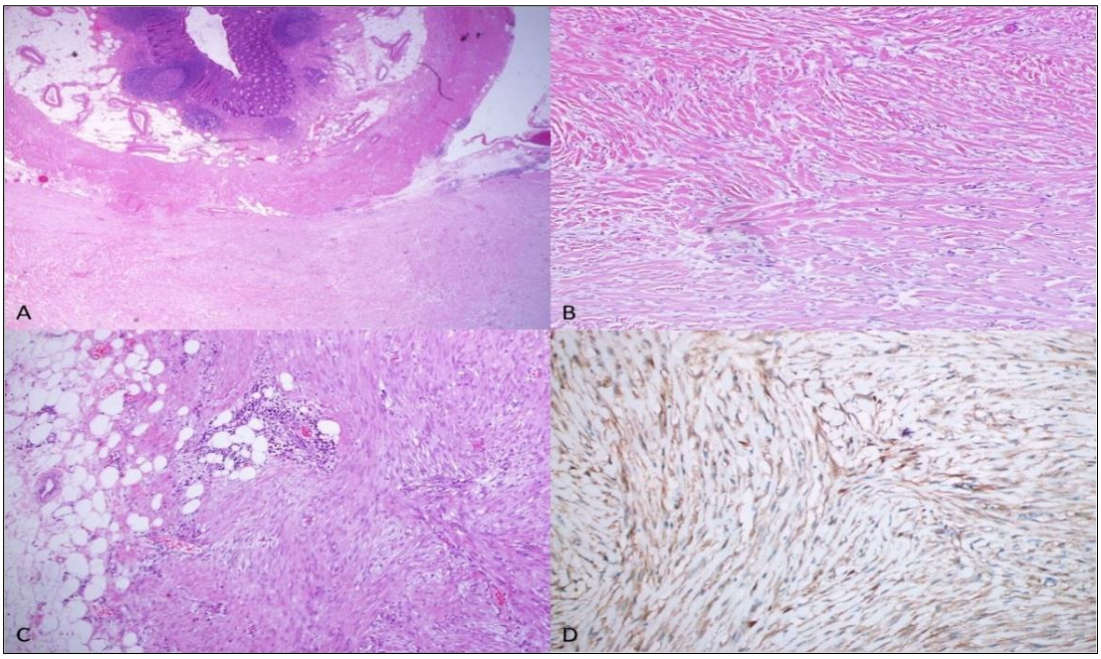

Figure 2: (A) Low power magnification showing desmoid fibromatosis arising from the appendiceal wall (H&E, 40x) (B) Bland spindle cells surrounded by collagenous stroma (H&E, 200x) (C) Tumor invading adjacent fat (H&E, 200x) (D) Tumor cells showing nuclear staining with beta-Catenin (IHC, 40x)

Figure 3: Visualization of CTNNB1 variant using integrative genomics viewer (IGV)

DISCUSSION

Intra-abdominal desmid fibromatosis is locally aggressive, deep-seated and arises from musculoaponeurotic structures, affecting the mesentery and retroperitoneum commonly [2]. It presents as an intra-abdominal mass and may mimic gastrointestinal tumour [2-5]. Intra-abdominal tumours can cause intestinal obstruction, fistula formation or gastrointestinal bleeding. Appendix and mesoappendix are very rare sites of mesenchymal neoplasms [1]. Clinically they present as painful or painless abdominal masses, abdomen distension or with complications related to the mass such as obstruction or acute appendicitis [1-9]. Only 3 cases of appendiceal fibromatosis have been reported in the literature [5]. Bhartiya *et al.*, reported a case of fibromatosis of the appendix in a 33-year-old female who presented with a right iliac fossa mass [2]. El Helou *et al.*, reported a case of giant mesenteric fibromatosis arising from the mesoappendix in a 34-year-old male who presented with

painless abdominal distension which is similar to the present study [9]. Zarbaliyev *et al.*, reported a 46-year-old male with appendiceal fibromatosis presenting as a painful abdominal mass [5].

Clinically, fibromatosis may present with a clinical picture like acute appendicitis or acute abdomen with perforation where emergency surgery is inevitable. Toydemir *et al.*, [1], in 2011 described a case of a 25-year-old patient with Cecal fibromatosis obstructing the appendiceal lumen and presenting with symptoms of acute appendicitis. The case report emphasized the possibility of rare aetiologies underlying common clinical symptoms and the importance of preoperative radiological assessment in such cases [1]. Asenov *et al.*, reported a case of aggressive fibromatosis of jejunum in a 27-year-old male patient who presented with a clinical picture like acute appendicitis and acute abdomen due to perforation [13]. Most cases are sporadic while some are associated with Gardner syndrome and FAP [4-9]. Other risk factors for fibromatosis include previous trauma, sites of previous surgeries and unopposed estrogen [5]. Fibromatosis is associated with recurrences due to their infiltrative nature, however they generally do not metastasize [9].

Imaging remains the mainstay for pre-operative investigations especially in patients presenting with non-specific symptoms [2]. CT scan is considered as the first-line imaging modality [2]. On CT, fibromatosis appears as an enhancing mass displacing or involving surrounding viscera which may appear well-circumscribed or often have irregular margins, reflecting its infiltrative nature [2]. MRI is more sensitive for accurate evaluation of the tumour and its relation to the surrounding structure [9]. Our case showed a well-defined mass without the involvement of surrounding structures.

Surgery is the first option of treatment to relieve symptoms [2-8]. Urgent surgical intervention has been done in cases of obstruction [6]. Radiotherapy is considered in cases with incomplete surgical excision or multiple recurrences [8, 9]. Other treatment modalities reported in the literature include targeted therapy, chemotherapy, hormonal manipulation and Nonsteroidal inflammatory drugs, and ultrasound-guided high-intensity focused ultrasound (HIFU) ablation [8, 9]. Non-surgical treatment modalities have shown an unpredictable outcome and are reserved for unresectable cases [6].

The histopathological examination is considered the gold standard for diagnosis supplemented by ancillary studies like immunohistochemistry and molecular analysis [4-9]. The most important diagnostic features of fibromatosis include myofibroblastic spindle cells with minimal pleomorphism, low mitotic activity, and abundant collagenous stroma [2-5]. In case of large masses, sudden increase in size, deep tumors or pain, extensive sampling is advised to look for features of malignancy [4]. Based on location, gastrointestinal stroma tumor (GIST) is the most common differential diagnosis [2-14]. It is important to differentiate fibromatosis from GIST due to different treatment and follow-up protocols [14]. An immunohistochemistry panel of CD34, beta-catenin, CD117 and DOG-1 will help differentiate between the two entities [5-7].

Diagnostically, CTNNB1 variant status has been identified as a desirable diagnostic criterion. Le Guellec *et al.*, [10], reported the presence of *CTNNB1* mutations in 88% of sporadic desmoid tumors, while none were identified in all other spindle lesions mimicking DF. Thus, evaluation of CTNNB1 variant can provide valuable diagnostic information, especially with small tissue biopsy lacking classical morphological features or equivocal β catenin immunohistochemistry.

CTNNB1 Variant identified in our patient is one of the most common variants in desmoid fibromatosis and has been described in ~50% of patients [15]. Studies suggest that tumors harbouring *CTNNB1* mutations have a greater risk for local recurrence and lower disease-free survival [12]. However, among CTNNB1 mutated cases, S45F tends to have the worst prognosis while T41A has significantly better disease-free survival [15]. The German Interdisciplinary Sarcoma Group (GISG) trial indicated that CTNNB1 mutation status could also help predict response to imatinib therapy (higher progression arrest CTNNB1 mutated vs wild type) [16].

Genomically, CTNNB1 and APC gene variants are mutually exclusive of each other. Importantly, most of the APC variants in desmoid fibromatosis tend to be germline in origin and are indicative of familial adenomatous polyposis (FAP). Thus, CTNNB1 mutation nearly rules out a possibility of FAP; while CTNNB1 wild-type patients should be subjected to further investigations to rule out FAP [15-17].

CONCLUSION

In general, intra-abdominal desmoid fibromatosis is very rare, with the appendix being an extremely rare location. GIST being the most common tumor in this location is a close differential diagnosis for fibromatosis. Histological diagnosis supported by immunohistochemistry and molecular analysis will differentiate the two entities. Radiology imaging is crucial for identifying the nature of the tumor outline and its relation to the surrounding structures. Surgical resection remains the mainstay treatment option in resectable cases. A multi-disciplinary treatment approach is crucial for patient care and management.

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Authors' Contributions:

Asim Qureshi and Hazwa Karathanathodi Hamza are responsible for data collection. Hazwa Karathanathodi Hamza and Nausheen Yaqoob, Prashant Deshpande prepared the manuscript. Asim Qureshi, Nausheen Yaqoob, Prashant Deshpande, Mirza Amanullah Beg and Ibrahim Al Haddabi reviewed the manuscript.

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Declarations

Competing Interests: The authors declare that they have no competing interests.

Ethics Statement:

We hereby state that informed consent authorizing data publication was taken from the patient. As per our center policy, case reports do not require clearance from the Institutional Research and Ethics Committee.

Patient Consent for Publication

Written informed consent was obtained from the patient and her parents for the publication of this report and any accompanying images.

No AI-assisted tools were used by any of the authors in the preparation of this work.

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