FIBROMATOSIS OF UNUSUAL SITES-A report of two cases

ABSTRACT

Fibromatosis is a group of tumors characterized by proliferation of fibroblasts and myofibroblasts that grow infiltratively but do not metastasize.Mesenteric fibromatosis itself is a rare entity,comprising less than 0.03% of all tumors, while scrotal fibromatosis is exceedingly uncommon, with fewer than 50 cases reported worldwide. The spectrum includes superficial and deep type based on location however both share similar histology but different molecular characteristics. Fibromatosis shows bland spindle cells arranged in long sweeping fascicles within a collagenous,infiltrative stroma without significant atypia or necrosis. Hallmark feature is strong nuclear beta catenin positivity adding distinction from reactive fibroblastic lesions.We are presenting two cases of fibromatosis arising at the unusual sites-one superficial and one deep, describing their clinicopathological features and discussing the pertinent differential diagnosis.

KEYWORDS

Spindle cells, superficial fibromatosis,deep fibromatosis, beta catenin.

INTRODUCTION

Fibromatosis comprise a heterogenous group of fibroblastic and myofibroblastic proliferations characterized by infiltrative growth and a propensity for local recurrence, despite their benign histological appearance.

The spectrum includes superficial and deep type based on location however both share similar histology but different molecular characteristics.

The overall incidence of desmoid-type fibromatosis is estimated at 2–4 cases per million population per year, accounting for approximately 0.03% of all neoplasms and about 3% of all soft tissue tumors.(1,2,3)The intra-abdominal variant represents nearly 8–15% of all desmoid-type fibromatoses, while abdominal wall and extra-abdominal forms constitute the remaining majority. Scrotal fibromatosis is exceedingly rare, with only sporadic case reports available, and its true incidence remains indeterminate.(4)

The present study highlights two cases of fibromatosis arising at the unusual sites-one superficial and one deep, describing their clinicopathological features and discussing the pertinent differential diagnosis.

CASE REPORTS

CASE 1- A 23 yearsold male presented with diffuse abdominal lump. On USG it was diagnosed as neuroendocrine tumor with high mitotic rate. Exploratory laparotomy was done and a large mesenteric mass adhered with bowel loop was excised. On gross examination, mass measured 20 x 15 x 7cm, which showed multifocal attachment to small bowel. Cut surface was tan, whorledand firm, without necrosis, cystic change, or hemorrhage.

On H&E, spindle-shaped fibroblasts with elongated nuclei and a benign appearance were seen.Microscopy shows unencapsulated, well circumscribed lesion with loosely arranged spindle cells with bland, oval nuclei and minimal cytoplasm in sweeping fascicles. There were also plump spindle cells with tapering ends, with oval, vesicular nuclei and moderate amount of eosinophilic cytoplasm. Splaying of fibres was seen. There were many thin-walled

vessels of varying caliber and perivascular hemorrhage. There were no cells with epithelioid features or any inflammatory cells, calcification, osseous metaplasia, necrosis, or mitoses. The tumor shows characteristic feature of melting insinuation into or through the muscularis propria. No polyposis was identified. Immunohistochemistry was performed - CD117, CD 34 were negative & B-Catenin, vimentin, SMA were positive. Hence GIST was ruled out.
A diagnosis of mesenteric fibromatosis was made.
Patient was given chemotherapy. However follow up was done and tumor recurred after one year.

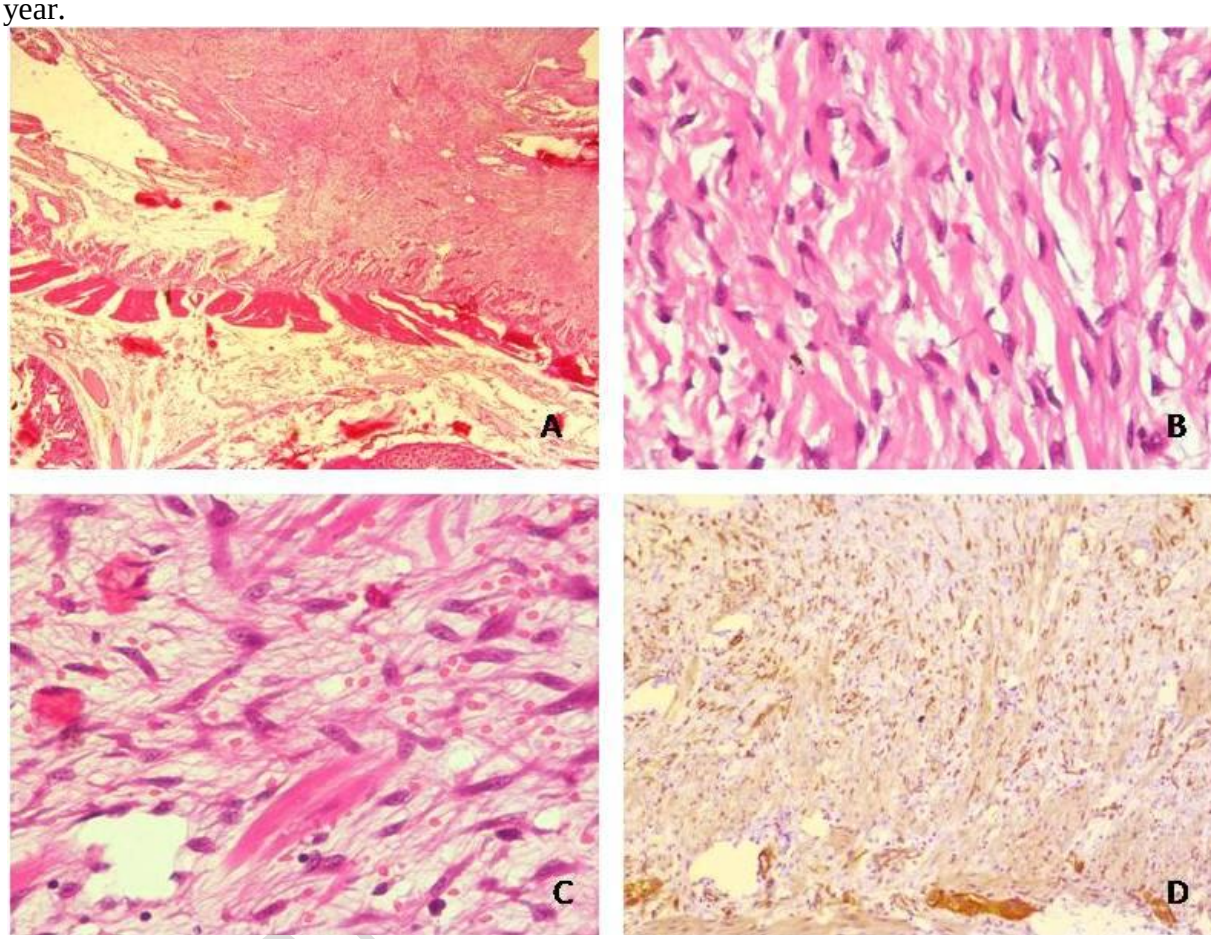

Figure1 – A:Mass lesion attached to the mesenteric surface(H&E x40), B: proliferation of spindle shaped cells (H&E x400), C:Showing splaying of the fibres (H&E x400), D: IHC-Beta catenin nuclear positivity (x100)

CASE 2- A 35 years old male presented with a slow growing mass in scrotum with surface ulceration. On gross examination excised mass was skin covered with ulceration measuring 5 x 5 cm. Preoperatively the testis with tunica were found free. There was no palpable lymphadenopathy.
On histology, tumor was composed of proliferation of uniform, bland spindle cells with an intervening collagenous stroma. No mitoses or necrosis was present. This lesion was found infiltrating within the dartos muscle. Minimal inflammatory infiltrate was seen. On IHC, tumor cells were found to be weakly positive for beta-catenin while they were negative for CD34, SMA, desmin and S-100. The cutaneous resection margin was free of the lesion. A diagnosis of pseudotumor was made.

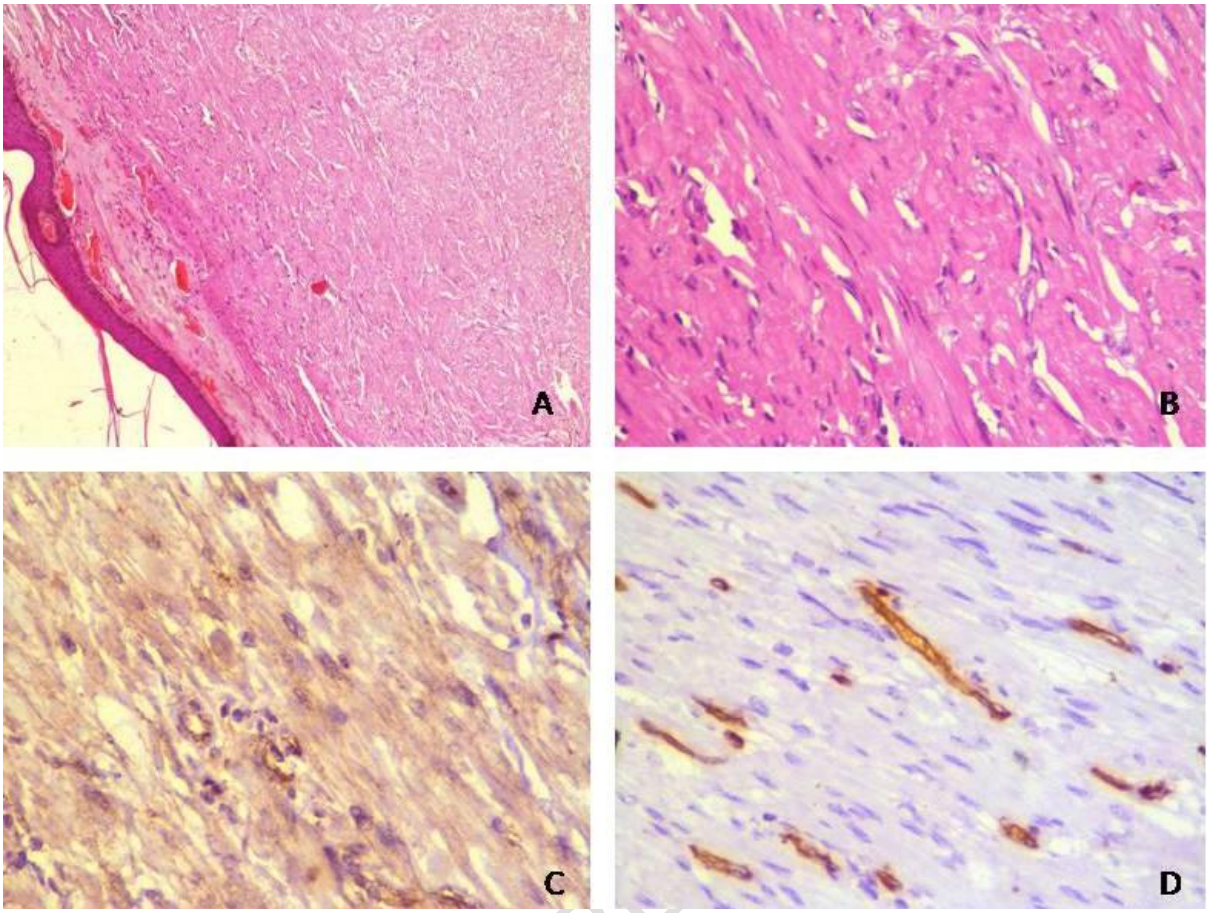

Figure2- A:Skin covered lesion with proliferation of fibroblasts (H&E x40),B: proliferation of spindle shaped cells (H&E x400), C:IHC-Beta catenin nuclear expression (x400), D: IHC-CD 34 negative with internal control (x400)

DISCUSSION

The term fibromatosis was coined by Stout in 1954.(5) Fibromatosis occupy an intermediate position between benign fibrous lesions and low-grade fibrosarcomas.

The spectrum includes superficial (fascial) and deep (musculoaponeurotic or desmoid-type) variants, with the latter often presenting diagnostic and therapeutic challenges due to their aggressive local behavior.

While fibromatosis most frequently involve the abdominal wall, shoulder girdle, and extremities, occurrence at unusual sites such as the intra-abdominal or scrotal regions is distinctly uncommon. Lesions in these locations may mimic other spindle cell neoplasms, both clinically and microscopically, leading to potential diagnostic pitfalls. Recognition of these rare presentations is therefore crucial for accurate diagnosis and optimal patient management.

Superficial fibromatosis typically occurs in middle-aged adults,whereas mesenteric fibromatosis is more common in young adults.(1)The age of our cases corresponds well with these reported peak incidences.Superficial fibromatosis predominantly occurs in males which is in agreement with our case.Mesenteric fibromatosis usually shows a female predominance,however,the presenting case occurred in a male patient, making it an uncommon presentation.

The etiopathogenesis of fibromatosis is multifactorial, involving a complex interplay of genetic, hormonal, and environmental factors. At the molecular level, most sporadic desmoid-type fibromatoses harbor somatic activating mutations in the CTNNB1 gene, which encodes β-catenin, leading to nuclear accumulation of β-catenin and dysregulated activation of the Wnt/β-catenin signaling pathway.[6] In patients with familial adenomatous polyposis (FAP) or Gardner syndrome, germline mutations in the APC tumor suppressor gene result in similar downstream β-catenin stabilization, explaining the predilection for intra-abdominal lesions in these individuals.(10)Thus mesenteric fibromatosis is associated with Gardner syndrome but in our case, no polyposis was seen.

Hormonal influences also play a contributory role, particularly estrogenic stimulation, as evidenced by the female predominance and the occurrence of abdominal wall fibromatoses during or after pregnancy.[6] Expression of estrogen receptor-β in some lesions supports this association. Additionally, trauma or prior surgical intervention has been implicated as a potential initiating factor, particularly in extra-abdominal and post-surgical fibromatosis, possibly triggering a reparative fibroblastic proliferation that fails to regress.

Fibromatosis shows intermediate biological behavior between benign fibrous tissue proliferation and fibrosarcoma. It shows local invasive behavior and tends to recur but does not metastasize. In fact, the course of intra-abdominal desmoid may be characterized by initial rapid growth, followed by stability or even regression.

Tumor can be asymptomatic when small, however with larger masses may present with features of intestinal obstruction, ischemia, perforation, hydronephrosis, ureteric obstruction and even aortic rupture due to pressure compression or infiltration. Primary IAF may arise ex novo but may occur secondary to trauma, hormonal stimulation. sometimes it may be associated with familial polyposis or Gardner's syndrome.In scrotum, the lesion is usually unilateral, but bilateral involvement has also been described. Clinically, it appears as a poorly circumscribed, firm to hard nodular thickening of the scrotal wall, sometimes leading to asymmetry or heaviness of the scrotum.

IAF is characterized by monotonous spindle cell proliferation in sweeping fascicles with variable cellularity. It's histological differential diagnoses are GIST, fibrosarcoma, leiomyosarcoma inflammatory myofibroblastic tumor depending on the location.

GIST is a close histological mimicker but has to be ruled out because of biological behavior and different line of treatment. IAFs are characterized by a spatially homogeneous broad sweeping fascicular proliferation of uniform cells with thin tapering eosinophilic cytoplasm with elongated delicate bland nuclei, associated with collagen deposition (often of keloidal type), low Mitotic activity, infrequent necrosis, hemorrhage, and myxoid degeneration. GIST shows thepresence of spindle as well as epithelioid cells with variable architecture or organoid fashion, mitotic activity, nuclear atypia, and myxoid or hyalinized stroma.(10) Necrosis and hemorrhage can also be seen. Ultra structurally IAF shows complete myofibroblastic/fibroblastic differentiationwhereas GIST originates from interstitial cells of cajal which have features of both smoothmuscle and neuronal differentiation.(7)Fibrosarcoma are malignant neoplasm offibroblasts showing marked cellularity with numerous mitoses and metastasize readily. Another differential Inflammatory myofibroblastictumors are characterized by a dense inflammatory cell component among myofibroblastic proliferation. Leiomyosarcomas is featured by larger tumor cells, cytologic atypia, increased mitotic activity, area of necrosis, and nuclear pleomorphism. The demonstration of melting insinuation is diagnostic of IAF a feature that is never seen in GIST, Sclerosing mesenteritis, IMT.

Superficial fibromatosis is characterized by bland spindle cells arranged in long sweeping fascicles within a collagenous stroma, showing minimal atypia and infiltrative margins. It demonstrates nuclear β-catenin positivity and variable SMA expression, while negative for

desmin, CD34, S100, and STAT6. The main differentials include solitary fibrous tumor (patternless architecture, CD34 and STAT6 positive), leiomyoma (cigar-shaped nuclei, desmin and h-caldesmon positive), fibrous pseudotumor (reactive fibroblastic proliferation with inflammation, β-catenin negative), fibrosarcoma (herringbone pattern with atypia and mitoses), neurofibroma (wavy nuclei, S100 positive), and leiomyosarcoma (cytologic atypia, mitoses, desmin and SMA positive). (8,9) Nuclear β-catenin expression remains the most useful marker distinguishing fibromatosis from these mimics.

IHC studies of various differentials-(7,9)

IHC Marker	GIST	Intra-abdominal Fibromatosis	Superficial Fibromatosis	Solitary Fibrous Tumour	Leiomyosarcoma	Fibrosarcoma
Vimentin	100%	100%	100%	Positive	Positive	Positive
CD117	88%	75%	Negative	Negative	Negative	Negative
CD34	42%	0%	Negative	88%	Occasional	Negative
SMA	63%	75%	Variable / Positive	Rarely positive	90%	Negative
Desmin	8%	50%	Negative / Variable	Negative	Positive	Negative
S-100	16%	0%	Negative	Negative	Negative	Negative
β-Catenin (nuclear)	5%	67% (familial) / 80% (sporadic)	Positive (nuclear)	22%	Negative	20%

CONCLUSION

Fibromatosis occurring at unusual sites such as the mesentery and scrotal skin is exceedingly rare and may present a diagnostic challenge due to its overlap with other spindle cell neoplasms. A definitive diagnosis requires meticulous histopathological evaluation supplemented by immunohistochemistry, with nuclear β-catenin expression serving as a key diagnostic marker. Recognition of this entity is crucial, as it exhibits locally infiltrative behavior without metastatic potential, thereby necessitating complete surgical excision and careful long-term follow-up.

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